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HEREDITY IN THE CLINIC.*

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To the biologists and especially the geneticists of this country, it must be little short of amazing that American clinicians have been so little influenced either in work or in thought by the stupendous advances that have been made in our knowledge of heredity since the turn of the century. For to the advances in genetic theory and practice, which began with the rediscovery by Johannsen in 1900 of Mendel's fundamental laws, American biological investigators have been among the most important contributors; moreover, our biological teachers and writers, too, have been busily engaged in disseminating widely the newer knowledge acquired both here and abroad. Researches like those of E. B. Wilson upon the cellular basis of heredity, of T. H. Morgan upon its physical basis in the fruit fly, of H. S. Jennings upon inheritance in unicellular organisms, of C. E. McClung upon the heredity of sex, of W. E. Castle upon blending inheritance, and of E. M. East upon inbreeding and outbreeding have yielded results that are famous the world around; methodology has been sufficiently covered by the writings of the scientists mentioned and by Raymond Pearl in his "Modes of Research in Genetics." Popular presentations, such as E. G. Conklin's "Heredity and Environment in the Development of Man," H. F. Osborn's "Origin and Evolution of Life," H. H. Newman's "Readings in Evolution, Genetics and Eugenics," and H. S. Jennings' "Prometheus" have made the main facts and theories easily accessible to any cultivated reader. Furthermore,

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the important recent works of foreign investigators of heredity (Johannsen, Bateson, Baur, Pearson, Punnett, Thomson, Goldschmidt) will be found available for reference in every large library. As I write, a new and important series of monographs by Johannsen, Brugsch and others is announced in "Die Biologie der Person." American biological thought is saturated with genetic considerations; they influence, too, to no inconsiderable degree, contemporary pedagogy and philosophy. Why then the apparent apathy of medical men with regard to the problems of inheritance? How can we explain the sluggishness of our clinics as far as efforts to apply the newer knowledge and technique to the solution of the problems of health and disease in man are concerned? There surely must be special reasons for the glaring contrast between the fiery enthusiasm for researches in heredity and development evident in the biological laboratories of every university and the coolness toward genetic questions and the concentration upon environmental influences that characterize activities in our hospitals and even in the laboratories of clinical research of our university medical schools.

This crass discrepancy between the biological and the medical interest in heredity has not been limited to America; it has been observable, and has already been subject of comment, in other countries. Various causes can be assigned, among them the following: (1) A temporary blindness to the significance of heredity for medicine owing to the fruitfulness of studies bearing upon environmental factors that favor health or cause disease (particularly since bacteriology, parasitology and toxicology have brilliantly emerged as sciences and since public and personal hygiene have been able to make such gigantic strides by attention to habits and surroundings alone without much consideration of endogenous determining influences within man himself); (2) the erroneous idea that for practical medicine genetic studies have only a limited application and chiefly then in domains relatively unimportant for human responsivity and accordingly for diagnosis and therapy (such as the color of the hair and eyes, the congenital malformations, and certain rarer pathologic conditions such as albinism, retinitis pigmentosa, and the heredofamilial diseases of the nervous and muscular systems); (3) the mistaken conception that emphasis upon heredity and constitutional makeup are necessarily conducive to pessimism in therapy and to a paralyzing fatalism (illustrated by past and present ideas of "stigmata of degeneration," of "congenital inferiorities." of "inherited susceptibilities" to infection, to insanity, and to crime); (4) the prevalence still of the old anthropocentric view that laws of inheritance that hold for plants and animals cannot possibly be valid for man (illustrated recently in this country by outbreaks of the so-called "fundamentalists," by the passage of laws against the teaching of evolution, by the famous trial at Dayton, Tennessee, and by many sarcastic comments upon Mendelians who are sup-

posed to believe that man mendelizes like a "pea," a "Chinese primula" or a "fruit fly"); (5) finally, the lamentable general ignorance among medical practitioners and investigators, themselves, of the possibilities of application of geno-analytical methods of study to human beings, to say nothing of their total lack of training, except in rare instances, in the use of such methods (genealogical-familial, mathematico-statistical, phenogenetic, and experimental). It is, in my opinion, to ignorance, to errors, to prejudices, and to misconceptions such as those just mentioned, and others that might be cited, that the backwardness and negligence of the clinical sciences in studies of inheritance must be attributed.

Fortunately, there are signs that clinical medicine (as well as anatomy and pathology) is awakening to its new opportunities; indeed, it is probable that before very long we shall witness a flaming revival of interest in the significance of heredity for medical theory and practice. Students of eugenics have stimulated medical men to a greater interest in racial hygiene; and even ardent advocates of euthenics have begun to realize that the variable influence of their measures depends upon the innate differences among human individuals. C. B. Davenport and his associates at the Eugenic Record Office have done much to further studies of human heredity; and in the "Journal of Heredity" edited by Poponœ as well as in the "Eugenics Review" (London) articles on human genesis frequently appear. Neurologists and psychiatrists, not surprisingly, have been leaders in the study of the human individual as a whole, as a psychophysical unit; they have in their studies of the relation of bodily structure to character and of general personality reactions begun to realize more fully the importance of inheritance both for body and soul. In H. H. Goddard's book on "Feeblemindedness" (1914) detailed information is given regarding hereditary relations. In Switzerland during the past fifteen years, genealogic studies of dementia præcox and of manic depressive families have been illuminating. At the fourth annual meeting of the Association for Research in Nervous and Mental Diseases (held in 1923) the whole program was devoted to a discussion of heredity. Endocrinologists investigating the influences of hormones upon body growth, body form, and metabolism have been compelled to go beyond the hormones and to consider chromosomal constituents and their origin. [See J. Bauer on "Constitution and Endocrines" (1925).] Even internal medicine, proper, has begun to pursue systematic genetic inquiries. F. Kraus, professor of medicine in Berlin, in 1919 published (in German) a "General and Special Pathology of the Person (Clinical Correlations)." which though difficult reading, may mark an epoch in internal medicine since in it, for the first time, a distinguished professor of clinical medicine gave evidence of a comprehensive grasp of modern genetics and of the importance of the distinction between the "phenotype" or realized person and

the "genotype" or inheritance pattern from which it is derived through a series of reactions with the environment. Two years earlier (in 1917) Julius Bauer, of Vienna, had published the first edition of his book entitled "The Constitutional Disposition to Internal Diseases" in which the inherited part of the constitution, earlier emphasized by another internist (Friedrich Martius), was duly valued. In the same year, a new journal, the "Zeitschrift für angewandte Anatomie und Konstitutionslehre," began to deal with problems of the anatomy and pathology of the constitution, and soon the general and special clinics in Central Europe began to busy themselves with investigations of the human constitution in health and disease. Attempts to understand the patient, not alone his disease, began to be made; as Brugsch puts it "personalism" must be adopted as a clinical slogan. In 1923, Baur, Fischer, and Lenz published their "Human Heredity"[1] and in 1924, George Draper, through whose influence a "Constitution Clinic" was established at the Presbyterian Hospital in New York City, published his book "Human Constitution; a Consideration of Its Relationship to Disease" in which the methods he uses in studying persons as a whole are described (under the captions Anatomic Panel, Physiologic Panel, Psychologic Panel and Immunologic Panel). In May of this year the same author has published an article on "Opportunities for the Clinician and the Pathologist Offered by Study of the Human Constitution." In 1923–1924, under the auspices of the Mayo Foundation, a series of six lectures on "Our Present Knowledge of Heredity" was delivered at each of six medical schools in the Middle West, occurrences that reveal strongly the growing conviction of the desirability of rapid dissemination of a knowledge of genetics among prospective medical practitioners and investigators. In the clinical journals, articles on the "clinical significance of heredity" and on "the practical results of the study of heredity" are becoming more numerous; even in some of the clinics for the medical and surgical specialties places are being made for "specialists on heredity within the specialty!"

How absurd the misconceptions and prejudices that have delayed the application of modern genetical methods to the solution of clinical problems are when they are carefully examined! For, in the first place, instead of having a limited application to practical clinical problems, the field of possible and, in time, profitable application is as wide as those of medicine and hygiene themselves. Every human being looked at by a clinician from the standpoint of genetics is a phenotype (realized person) who has become what he is by starting as a fertilized egg cell (zygote), which arose, in biparental reproduction, from the union of a sex-cell or gamete from the father (spermatozoön) with a sex cell or gamete from the mother (ovum).

[1] Menschliche Erblichkeitslehre.

The materials of which this zygote was composed entered into reactions with oxygen, foods, and other chemical substances outside the zygote, first under the influence of the physical environment of the mother's uterus, later in the world outside. Whatever phenotype the zygote develops into (as a fetus, an infant, a child, an adolescent, or an adult) must depend, obviously, first upon the composition of the gametes that fuse to form the zygote and second upon the influences (chemical, physical, psychical) outside the zygote, which act upon it. Each gamete consists of nucleus and cytoplasm, the nucleus in turn containing chromatin threads shaped something like croquet hoops and known as chromosomes. Each chromosome consists of rows of beadlike masses that contain discrete packets of diverse chemical substances (collocations of chemical molecules); geneticists call these packets "genes." The chromosomes from the two parental gametes arrange themselves in pairs, so that each packet or gene from the paternal gamete meets in the zygote a corresponding packet or gene from the maternal gamete, the two chromosomes thus forming a set of pairs of genes. The chemicals in one member of each pair may be the same as those in the other member of the pair; more often, the chemicals though related differ somewhat in the two members of each pair; but, in any case, the genes appear to be arranged definitely in a series, like pearls on a string. The way these genes are arranged in the chromosomes in a linear manner is most important for our newer knowledge of heredity and development. In certain organisms (like the fruit fly) several hundreds of the packets have been definitely located so that topographic maps of the chromosomes and their contained genes are now available. The total aggregate of genes definitely arranged constitutes the so-called "genotypic pattern." Gradually the arrangement of the genes in the chromosomes of other organisms is being discovered; we already know something about the arrangement of genes in human chromosomes. The so-called laws of heredity have to do with the rules of distribution of genes from the father and the mother to the zygote and with the interrelations of genes belonging to different pairs within the chromosomes of the zygote. For a time, it was supposed that each gene corresponded to some particular feature in the developed organism that was spoken of as a "unit character," but later studies have shown that this was an error. It is now believed that the genes interact with one another and with the substances about them over long periods, so that the phenotypic characters that emerge are distant and indirect results of these many interactions. Thus, the red color of the eye of a fruit fly is said to be dependent upon the interaction of at least fifty genes, alteration of any one of the fifty preventing the production of the red color! Moreover, the way the genes interact with one another and with their cytoplasmic surroundings depends to a large extent upon the environment, the development that

occurs depending not alone upon the genes but also upon their surroundings to which there is never-ceasing adjustment. It must be clear then that every developed characteristic of a phenotype depends upon the genotypic pattern in the zygote on the one hand and the influences acting on that pattern from without on the other. A given genotypic pattern appears to be capable of giving rise to many different phenotypes provided it could be exposed to many different conditions during development. What an animal or a man has become depends then only partly upon the genes present at the start; the surroundings of the genes are also determining of the characteristics that ultimately emerge. No characteristic of the phenotype is independent either of the genotype or of its series of environments. Obviously then, the field for genetic studies of given phenotypes is as wide as the total sum of their manifold characteristics. The study of heredity in man is not limited to the investigation of peculiar variations or of rare anomalies and diseases; it is applicable to every detail of human structure and of human function, whether "normal" or pathologic. No less than two hundred and twenty-three heritable anomalies have been described in man already; in time many more will doubtless be recognized.

The prejudices against studies of heredity and of constitution because they are supposed to compel pessimistic and fatalistic ideas in clinical medicine is, from what I have just said, entirely unfounded. Though it is true that the genotype with which an organism starts has much to do with the development that follows, it is not wholly decisive. The limits set by the aggregate and arrangement of constituent genes certainly cannot be transcended, but the possible variations within the limits are much wider than was formerly thought. Nothing is absolutely fixed or foreordained within those tolerably wide boundaries. The genotype does determine a certain norm of reaction, but the results of reaction will differ according to the influences and substances reacted with. An organism develops through a series of successive phenotypes, each member of the series being the resultant of adjustments of the preceding member to the environment. We are learning how to change human phenotypes artificially to their advantage; that is one of the functions of medical therapy. Witness, the change in a hyperthyreotic phenotype on excision of one lobe of the thyroid, or that in a hypothyreotic phenotype on feeding thyroxin, or that in a diabetic phenotype producible by hypodermic injections of insulin! Here is room for optimism surely, for the more we know accurately of phenotypes and their origin from genotypes interacting with environments, the greater will be our power to influence them favorably. Though the "hand of the past is found to have a heavy grip" we should not forget, as Thompson has pointed out, "the other side of heredity: the persistence of the stable; the conservation of advantageous qualities; the continual emergence of the new; and the influence of nurture in

determining the degree of development to which hereditary nature attains."

The hindrance to genetic research in man because of the persistence of ancient anthropocentric conceptions will, we can feel sure grow gradually less. Medical students, today, all study general biology and, in most states, they study evolution too. As they become physicians, their biological knowledge will protect them from the fallacious idea that the laws of life for man must be wholly different from those that obtain for animals and plants. They will not be deterred from the study of heredity in man because he does not mendelize precisely as does the pea or the fruit fly, particularly when they find that man does actually mendelize.

When they find how genetic studies extend the domain of etiology to the investigation of causes that are prezygotic or progametous in the time of their influence and to researches into the origin of pathologic alterations of genes; when they learn that the genes are units fully as important for true medical conceptions as are the units known as cells, as molecules, as atoms, as ions or as electrons; when they come to understand that correlations regulated by genes are no less important than are nervous and hormonal correlations, that they are indeed even more fundamental than these; when they realize that genotypic patterns in zygotes are the keynotes to the peculiarities of all human constitutions and to the individual features of all human personalities; when they grasp the idea that no two genotypes are ever alike (except in the case of identical twins) and that every genotype, being unique, occurs only once in the world and ends with the death of the phenotype to which in reaction with environmental influences it has given rise—no fundamentalist opposition and no state or national law will deter them from views that are based on sound biology. They will be eager to participate in the discovery of as many genes as possible in human genotypes and of their influence in the production of individual human phenotypes, both normal and pathological. They will desire to learn how pathologic genes originate and how their malevolent influences can be counteracted. For they will quickly recognize that in the future of medicine studies of "gene physiology" and "gene pathology" are destined to play a very important rôle.

The technique of genetic investigation is very complex. Even genealogical and familial studies, if they are to yield reliable results, require most painstaking research. The mathematical-statistical evaluation of the findings demand a training that only relatively few have thus far gained. The analysis of human genotypes for their constituent genes and the construction of their patterns will afford work for many generations of medical investigators. To discover all the influences that a given normal or pathologic gene can exert, to learn by phenogenetic studies the relations of single genes to realized characteristics, to find out what happens to a human organism

when a gene ordinarily present is absent or altered—these are problems that are full of interest and should be stimulative of ardent research. Already important results for the clinics are being achieved, notably as regards osteogenesis imperfecta (in which abnormal genes seem to be responsible for changes in the whole mesenchyme), hemophilia (in which pathologic genes seem to be responsible for the faulty formation of thrombokinase in the body cells), and chondrodystrophia (in which changes in the growth of bone and cartilage, alterations of the physiognomy, and modifications of sexuality and of the psyche are all being led back in their causation to a faulty genotypic pattern, perhaps to a single pathologic gene).

Many have thought that heredity in man is not susceptible to experimental approach. Because human beings, genetically considered, are immensely complex "polyhybrid heterozygous bastards" and because we cannot control matings in them as we do in guinea pigs, rabbits, or garden peas, it has been assumed that experimental research can be of no value for human heredity. But no person denies the value for man of experimental research in the physiology and pathology of the heart, of the liver, and of the brain carried out on animals with cautious transfer of the results by analogy to the physiology and pathology of man. We have learned much regarding the conduction mechanism in the human heart, regarding the possible origin of cirrhosis of the liver in man, and regarding cerebrospinal localization in man from experiments on animals. Why then should we assume that genetic facts learned from animal experiment are wholly inapplicable to man. Who can doubt that researches on the heredity of tumors and of susceptibility to tumor transplantation such as are carried on at the University of Chicago, at the Rockefeller Institute in New York, and at the Wistar Institute in Philadelphia will prove to be of importance also for man? Studies in animals, too, of inherited susceptibility to various infections, to endocrine disturbances like goiter, and to various other pathologic states should all, in time yield results that can be utilized to illuminate the influences of heredity in human beings also. Disease among animals, though less prevalent than in man, occur in sufficient variety and frequency to warrant continued search for them and the study of their genotypic relationships when found. Comparative medicine can thus be forced to contribute ever new facts that can throw light on human medicine.

The subject could be pursued much further did time permit. I hope, however, that the ground already covered, will suffice to show how important a knowledge of the science of heredity and the application of its technique can be for the tasks of the clinic. As K. H. Baur has pointed out, the doctrine of endocrinology quickly conquered medical thought, largely because it harmonized with the localistic principles of the morphologists (in that the increta were

associated with definite organs) as well as with the endeavors of physiologists to study everywhere chemical reactions. The doctrines of heredity have been less congenial to medical thinkers because they were unprepared for it by their earlier education. But the younger men entering medicine today have had a better biologic training than their predecessors. And you will agree, I believe, that it cannot be long before the repercussion of the theory of heredity upon medicine will become much more noticeable than hitherto.

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ANESTHESIA FROM THE STANDPOINT OF THE SURGEON.*

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This paper will consist of a brief discussion of my reactions to anesthesia as judged from the experience of the past four years on

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my services in the University and Misericordia Hospitals. During that time we have had about 6000 operations, covering practically the entire field of surgery. Naturally, the surgeon is interested in anesthesia; he is responsible morally and usually legally for any carelessness in its use. He knows his patient and must select the anesthesia from such knowledge. We are accustomed to having anesthesia mostly given by a nurse trained in anesthetic methods. I cannot praise too highly the work of our regular nurse anesthetists. Their technique is wonderful, and it is surprising how much real knowledge of the action of anesthetics they have acquired from reading the standard works and periodical literature.

The particular anesthetic to be used will depend upon the operation, the condition of the patient and in the case of local or regional anesthesia the ability of the surgeon to master the technique. Ten years ago practically every major operation which I did was performed under open-drop ether anesthesia. Today the reverse is the case, ether being given much less frequently and mostly when nitrous oxid or ethylene is insufficient to afford relaxation and ether must be added. We use the Gwathmey apparatus. The following table shows the method of anesthesia used on my service in the University Hospital during the first and fourth years of the present régime:

TABLE I.

	1922–1923, per cent.	1925–1926, per cent.
Local	10	22
Ether	43	11
Nitrous oxide-oxygen	25	33
Ethylene	0	15
"Gas"-ether	17	14
"Gas"-local	2	4

The combination of gas-local, using either nitrous oxid or ethylene gas, is represented too low, because during the past four or five months we have been using novocain in the abdominal wall in practically every case of gas anesthesia. The per cent given means those cases started under local and the gases subsequently added, because of failure to anesthetize.

Local Anesthesia. Our use of local anesthesia alone has about doubled, and at the present time practically every abdominal operation is done under gas anesthesia plus extensive infiltration with novocain (0.5 per cent). One is enabled to stop the inhalation anesthesia as soon as the peritoneum is closed and the patient is conscious and talking rationally before leaving the operating room. I have had but little experience with splanchnic anesthesia, but have begun its use recently with satisfactory anesthesia, although the fall in blood pressure is rather alarming. We have used the posterior method of Kappis.

Operations for chronic appendicitis and hernia are frequently done

under local anesthesia. Inter-rib drainage of empyema and colostomy or enterostomy for intestinal obstruction are always operated upon under local anesthesia. I do not like local anesthesia alone for gall bladder or stomach operations, but prefer the gas-local combination. In this group the splanchnic anesthesia has its best application. In acute appendicitis we start the gas and drape and prepare the abdomen. Local anesthesia of the skin and muscles is then done and after the appendix is removed and drains placed the gas is stopped. I hesitate to infiltrate the mesentery of cecum or appendix, fearing the introduction of septic material on the point of the needle.

Local anesthesia has a wide application and should be studied and practised by every surgeon, so that it can be used alone or in combination in nearly every case requiring prolonged anesthesia. The anesthetic is a mental hazard for most patients, and in nearly every proposed operation, except in the case of those desperately ill, I am called on to discuss this point with the patient. Nearly every patient dreads ether, even fears it, and the discussion has been made easier for me by my ability to announce that I rarely use ether and will not do so unless forced into it. We might tell the patient that the risk in spinal anesthesia is as 1 in 500; in chloroform, 1 in 3000; while in ether it is only 1 in 16,000; but still they are not convinced. I like to operate with the patient under ether anesthesia because of the greater relaxation, the ease of exposure and the ability to "speed up." On the other hand, the ward nurses do not like it because of the frequent vomiting, the need of physical restraint in many cases and the detailing of separate nurses to watch the patient. In a ward where patients are coming down from the operating room every half hour or so this is an important item in ward management.

Ether. Ether is a safe anesthetic for the average anesthetist and for the patient, with certain exceptions. Until recent times the literature was voluminous and concerned with the technique of administration. Even now the special journals on anesthesia are mostly filled with articles bearing upon the use of ether and especially with experimental data bearing on its effects. And yet, in large clinics the use of straight ether is constantly diminishing. As has been said, the influence of the patient has had much to do with this, but there is another reason. Minor operations can be done readily under local or gas anesthesia, and the same may be said for simple major operations, such as hernia or chronic appendicitis. But the sick patient is the important one; he furnishes the mortality, that dread of all well-run clinics, and experience has taught that the prostatic, the depressed cardiorenal patient, the diabetic, the jaundiced, the patient with intestinal obstruction or acute appendicitis do not stand ether. I am not able to discuss for you the

complexities of acidosis, ketosis, ammonia disturbance, hyperglycemia and so forth. Something, however, must be known about them and certain tests carried out if we are to evaluate the risk from anesthesia.

For all practical purposes the determination of acidosis may be done by estimating the plasma CO_2 volume. The blood plasma of the normal adult contains from 50 to 65 volumes per cent of CO_2 gas as bicarbonate. If this is below 30 per cent the patient is in serious danger. Even at 40 per cent the condition is serious, and ether if prolonged will promote the production of lactic and other nonvolatile acids which cannot be neutralized Stehle and Bourne believe that ether acidosis results from a disturbance in the phosphorus metabolism. With the increase in the hydrogen-ion concentration, the colloids of the cells will absorb water and the urinary output decrease so that further poisoning results.

In the diabetic the acidosis is generally termed ketosis, and it is well known that ether aggravates the condition by disturbing the metabolism of carbohydrates and should not be used In the jaundice group the depressed liver loses its protein detoxicating power and the kidneys must bear a heavier burden. Ether alters and depresses the functional activity of the liver and hence should not be used to any degree in the jaundiced patient. We all know that the patient past middle age is a greater risk than the young adult, and hence the results of some very interesting experiments published by MacNider upon the stability of the acid-base equilibrium of the blood in animals of different age periods when anesthetized by ether is important. In puppies and young adult animals it was found that the physiochemical state of the blood was stable and practically uninfluenced by the ether, whereas in old adult dogs it was found that the acid-base balance of the blood was not stable. There occurred a marked reduction in urine formation, with the appearance of albumin and casts in the urine and more rarely diacetic acid; the elimination of phenolsulphonephthalein was markedly reduced. Even anuria occurred. It seemed that the kidney was furnished a blood of such altered composition that it failed to functionate in a normal fashion. Barbour and Bourne, of the department of pharmacology, McGill University, believe that ether oliguria and anuria are probably due more to thickening of the blood than to any renal factor. They found that the preanesthetic administration of water or hypotonic solutions reduces markedly the blood concentration produced by ether.

We spoke of vomiting as a postoperative trouble from ether. On the second day the patient experiences certain pains which are traditional as the inevitable "gas pains." Many remedies have been suggested but I believe the anesthetic itself is the important factor. This is confirmed by a paper recently published by Miller,

from the department of pharmacology, State University of Iowa. He found that after ether or chloroform anesthesia the stomach remained relaxed, whereas the small intestine early shows exaggerated peristalsis; the colon soon after anesthesia is withdrawn develops a high tonicity which may approach spasticity. This high tonicity of the colon acts as a functional, partial obstruction, favors the accumulation of gas and fluid above this level and the exaggerated peristalsis of the small intestine above the partial block could cause the so-called "gas pains." On the other hand, the usual anesthesia with ethylene and oxygen produces relatively little effect on the movements of the gastrointestinal tract, no inhibition of tone or of contractions occurring with this form of anesthesia. Tone is lowered, peristalsis ceases and segmental contractions are much diminished. This depression usually lasts one hour or longer.

Pulmonary Complications. The so-called ether bronchitis or ether pneumonia is stressed by many surgeons in explaining the reason for these complications to the relatives of the patient. If a patient, not in an acute stage requiring immediate operation, is operated upon while suffering from a cold the surgeon can expect trouble and is responsible for it. But in the average case the ether itself has little influence upon the development of pulmonary complications. From September, 1925, to September, 1926, 1132 operations were done on my service in the University Hospital, and there were 12 pulmonary complications (1.1 per cent). The anesthetics used in these cases were ether, 2; nitrous-oxid ether, 1; nitrous oxid, 2; ethylene, 1; local, 2; nitrous oxid local, 2; ethylene local, 2. This was a percentage of 1.4 for the ether cases, 0.9 for the local anesthesias, 0.7 for ethylene and 0.6 for nitrous oxid. After inhalation anesthesia alone (ether, nitrous oxid or ethylene) the percentage of pulmonary complications during this year was 0.9 per cent, whereas when local anesthesia was used, with or without combinations (with ether, nitrous-oxid oxygen or ethylene) the percentage was 2.2 per cent. One of the ether cases followed endotracheal anesthesia resulting in multiple lung abscess. I do not like this form of anesthesia but was asked to use it.

Recent writers, especially Cutler and Hunt, believe that except for acute bronchitis the pulmonary complications are mostly due to emboli. Hence rough handling of tissue and the crushing of large veins is as important as the anesthetic. The high incidence after local anesthesia may be due to the production of thrombosis in veins injured by the needle puncture.

Recent studies on atelectasis of the lung tend to show that hypostatic congestion following the collapse may be converted into a pneumonia by bronchial infection. The atelectasis or collapse need not be total or "massive," but may be partial in a lobe. This may be a cause of postoperative pneumonia.

TABLE II.

	Operations.	Pulmonary complications.	Per cent.
1922–23	844	12	1.4
1923–24	1076	9	0.8
1924–25	1021	13	1.3
1925–26	1132	12	1.1
Total	4073	46	1.1

During the four years from September, 1922, to September, 1926, we had 4073 operations on my service in the University Hospital and had 46 pulmonary complications (1.1 per cent), with a mortality of 37 per cent. This constituted about 10 per cent of the mortality of the service, and hence is a factor to be reckoned with. Naturally most of the patients probably would have died from their disease, but the difference between the pulmonary group (37 per cent) and the mortality in those without pulmonary complications (3.8 per cent) shows the importance of this factor.

TABLE III.

	Cases.	Deaths
Acute bronchitis	10	0
Bronchopneumonia	15	7
Lobar pneumonia	6	3
Pulmonary embolus	11	4
Lung abscess	3	3
Massive collapse	1	0

In a study of this subject by Ravdin and Kern from our hospital it was found that seasonal variation, incidence of subnormal temperature after operation, sex and age, location of the ward and duration of anesthesias, all played a part. If to these we add the still greater factors of small emboli and partial atelectasis, we see that the anesthetic alone must not be held responsible if we exclude the important factor of an existing "cold" antecedent to inhalation anesthesia.

Nitrous Oxid and Ethylene. For many years nitrous oxid and oxygen have been used in our clinic, and its use was gradually extended, until last year 33 per cent of the operations were done under this anesthesia. When ethylene was brought out, and especially after Dean Lewis popularized its use, we began using it. Last year 15 per cent of the anesthesias were by ethylene, making a total of 48 per cent for the "gases." I will not dilate at any length upon these anesthetics except to say that our anesthetizers start with nitrous oxid; if relaxation is not soon attained they switch to ethylene and if the patient is still unrelaxed they add ether to the gas mixture. In about 30 per cent some ether was necessary. At the present time the addition of ether is rarely necessary, owing to the combination of local anesthesia with gas as a routine in abdominal operations. I know of only one death that might be traceable directly to gas anesthesia, a case of intestinal

obstruction from a gall stone, the patient dying suddenly on the table from cardiac failure. Once I had a similar death under spinal anesthesia, once under local anesthesia and several times from ether.

Leake, of the University of Wisconsin, concludes that: "Ether causes: (*a*) An immediate and marked fall in both the blood pH and bicarbonate, leading, if the etherization is sufficiently prolonged, to an uncompensated alkali deficit; (*b*) this response is independent of respiratory variations under the influence of ether, and is not caused by the formation of ketone bodies nor lactic acid; (*c*) there may be a ketosis developing several hours after the withdrawal of ether, due probably to deranged carbohydrate metabolism, which is apparently related to the depressing effect of ether on the normal insulin secretion of the pancreas."

Nitrous oxid and oxygen anesthesia necessitates some degree of anoxemia, and this is responsible for certain changes which are, according to Leake, "an initial increase in the pH with inconstant changes in the CO_2 content." The reaction is not as marked as after ether.

The effects of ethylene-oxygen anesthesia on the blood reaction were found to be even less than after nitrous-oxid oxygen, because it is possible in most cases to keep the oxygen saturation of the arterial blood within normal limits and hence there is no anoxemia. If anoxemia is present Leake finds that: "There is an initial mobilization of blood alkali, followed by a gradual tendency toward an uncompensated alkali deficit. If no anoxemia is present the pH and CO_2 content of the blood both fall gradually, but not beyond normal limits after forty minutes' anesthesia."

I would also call attention to the fact that local anesthetics, unless used in toxic doses, have no effect on the blood reaction.

Cases with high blood pressure and poor cardiac risks are ordinarily excluded from gas anesthesia. In the former we prefer local anesthesia or, if necessary, ether if the kidneys can be protected. In cases with a poorly compensated heart lesion local anesthesia should be used and care taken regarding the depressing effect of the preliminary morphin dose.

Cardiac Factors. We are rarely afraid, however, of the cardiac factors in deciding upon anesthesia. The patient and his family physician worry a lot about the condition of the heart and frequently I have had to combat the statement, "My doctor says I should never take ether because of my heart." Many murmurs are purely functional, and even the organic leak or stenosis causes no anxiety if compensation is present. Auricular fibrillation requires study and preoperative treatment. The use of the blood pressure apparatus and renal function tests are of paramount importance in eliminating or minimizing the cardiorenal impairment. Naturally one would not operate needlessly upon a case of angina pectoris.

Kidney Factors. More important than the heart is the condition of the kidneys. Without going into the theoretical aspect of the question, I find it advisable to know certain things about kidney function in all patients past middle age and to watch this function in all sick patients before and after operation. Intake and output charts are invaluable, blood urea and nitrogen tests, and in the ordinary urinalysis the search for pus or blood cells in the urine is routine with us. I think that blood pressure determinations are valuable because an adequate maintenance of the pressure is essential to both glomerular and tabular activity. All of the changes in the rate of renal secretion, which occur in individuals whose kidneys were functioning normally previous to operation, can be explained as the consequence of a rise or fall of the blood pressure and of a simultaneous variation in the velocity of the blood in the renal vessels.

Richards and Schmidt, of the University of Pennsylvania, have demonstrated that the glomeruli of the frog's kidney have periods of constricted closure alternating with periods during which they permit the flow of blood. Although this introduces a new factor into the problem of urinary secretion, it is conceivable that in individuals whose blood pressure has dropped considerably below the preoperative level the resulting circulatory stasis produces in effect a continued glomerular constriction. No doubt you are familiar with Mott's rule, which is supposed to furnish an index of one phase of the anesthetic risk. It is based on the relation of pulse pressure to diastolic pressure. It reminds us that pulse pressure, as an indication of cardiac strength, must be sufficiently high to compensate for a deficient kidney function because the addition of fluids is useless if the pressure cannot push them through the kidneys. We find that ordinarily glucose solution given intravenously is a better diuretic than the drugs, such as caffein, which are so often used.

I do not need to caution you of the danger of ether in operations on the chronic prostatic. Local anesthesia and ethylene, parasacral anesthesia, or even spinal anesthesia, have the preference. The age of the patient, the susceptibility to respiratory complications and the surety of some degree of kidney damage are sufficient reasons.

General Considerations. The physician or surgeon must not be led into ascribing an undue importance to the action of the anesthetic agent. Clinical experience and even pharmacologic investigation show the relative harmlessness of anesthetics properly given in the young adult who is not toxic. Many of you no doubt use ether as a routine and can point to your series of successful operations, but I am sure if you card index your patients suffering with diabetes, jaundice, depressed kidney function, toxic goiters, hypertrophied prostate and acute appendicitis, and study the deaths you will note that usually they die from an aggravation of the lesion existing before operation. If you will properly study these patients,

properly prepare them, use local anesthesia to the limit and follow up the postoperative treatment with "floods" of water you will find that in the next series the mortality will be cut enormously. The principle of anociassociation, devised by Crile for the toxic goiter patient, is applicable to all and we must never minimize in our minds the inherent fear which the patient has of operations and anesthesia, and the drive of this fear on the central or sympathetic nervous system.

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SUMMARY OF EXPERIENCES UP-TO-DATE IN THE SURGICAL TREATMENT OF ANGINA PECTORIS.*

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The surgical treatment of angina pectoris is based on the hypothesis that the stimuli which give rise to the symptom pain arise in the heart and are carried by some nervous pathway to the spinal nervous system where these impulses overflow and stimulate the somatic sensory neurons supplying the upper thorax, arms and neck. The surgical act is aimed at division of this nervous arc, thus preventing the patient from recognizing the symptom pain. As the pathologic condition which causes angina pectoris is still unknown, there is no intention of eradicating the disease by surgery. It is a method of treatment which is purely symptomatic, and therefore identical in purpose with the division of the sensory root to the Gasserian ganglion in cases of trifacial neuralgia.

The operative treatment of angina pectoris was first proposed in 1899 by François Franck. It was first practised by Jonnesco in 1916. The operation performed by Jonnesco was an elaborate procedure, as he felt it was necessary to remove completely the upper three cervical ganglia and the first dorsal sympathetic ganglion on both sides. Chiefly because of the technical difficulties and in spite

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of the fact that Jonnesco's first case presented a most satisfactory result, the operative treatment of angina pectoris was not popularized. In 1923, Coffey and Brown, of San Francisco, claimed that their experience on 5 cases showed that removal merely of the superior cervical sympathetic ganglion or even division of the main branch from this ganglion to the heart sufficed to ameliorate the pain in cases of angina pectoris. The successful results reported by these investigators using such a simple procedure led to a very general practice of surgical operations upon patients suffering with angina pectoris. Whether the procedures above mentioned or the many variations of them, or even the division of those branches from the vagus nerve thought to be the depressor nerve, are of value in the treatment of angina pectoris is still under dispute. Even if these procedures fail ultimately to prove of great practical value in clinical medicine, the stimulation toward the study of cardiac pain and the proper innervation of the heart will have been of great value to the profession. It is perhaps unfortunate that a certain phase of this endeavor could not be studied experimentally in animals, but here, as in comparable instances in medicine where pain is the chief symptom, we must conduct our final investigations upon human beings themselves.

Before we turn to a discussion of the results achieved by the many varied procedures proposed in an effort to see which procedure has been most successful in abolishing the symptom pain, we must orientate ourselves by an appreciation of the nervous connections of the human heart. Figure 1 shows schematically the general relationships. The total innervation of the heart is comprised in the paired vagi and sympathetic nerves. Physiologic experimentation in which these nerve trunks and their cardiac branches have been completely divided prove beyond doubt that there are no other nervous connections between the heart and the central nervous system. Similar isolation experiments involving only one or the other pair of nerves or experiments with incomplete separation of the total nerve supply have given us definite information concerning the functions of these nerves. It has long been known that certain of the vagal fibers constitute the so-called depressor nerve, and it is known that in this nerve are afferent fibers and that stimulation of the central cut end will slow the heart beat. These are the only fibers in the cardiac portion of the vagus system which are afferent. As regards the sympathetic nervous connections, we have equally constant and accurate information. It is possible to trace histologically sensory fibers in the sympathetic system, and investigators have proved that some of these sensory fibers in the sympathetic connections run up from the heart as high as the middle cervical ganglion. No sensory fibers, however, have been found above this point, and we may be certain that the superior sympathetic ganglion and its branches have a purely motor function. These sensory

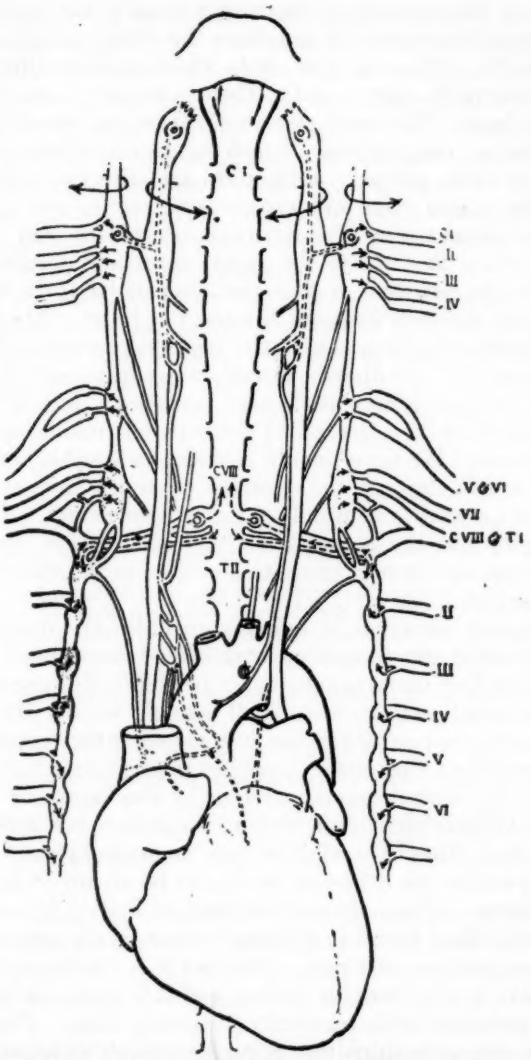

FIG. 1.—Connections of the heart with the central nervous system. The paired vagi are shown next to the cord with the ganglionated sympathetic chains external to the vagi. The connections of the sympathetic ganglia with the spinal nerves are drawn in. The origin of the depressor nerve in the superior sympathetic ganglion and in the upper ganglion of the vagus are represented with these fibers drawn in with dashed lines in the vagi and sympathetic ganglia. These fibers then branch away with the superior laryngeal nerve and finally travel free in the neck to end in the suprasigmoid portion of the aorta. The fibers running from the three cervical sympathetic ganglia medially and downward represent structures commonly called the upper, middle and lower cardiac nerves. These nerves are joined by many vagal fibers and fibers from the stellate and sometimes second dorsal ganglia to form a great network both in front and behind the aorta and base of the heart, in which in turn are embedded many sympathetic ganglion cells. Except for the connection of the vagi with the central nervous system in the brain stem, the connections between the stellate ganglion and the spinal cord at the level of the first dorsal nerve represents the only proved connection between the heart and the central nervous system.

sympathetic fibers, whether reaching primarily the middle or the inferior cervical sympathetic ganglia or the stellate ganglion, eventually end in the stellate ganglion from which emanate direct sensory fibers leading to the spinal cord. There is no such spinal connection above this level. The confirmation of this work, which was originally studied by Langley and Gaskell by degeneration experiments, has been recently given by Edgeworth and Ranson. In the illustration the paired vagi and sympathetic nerves are represented beside the spinal cord. The recurrent nerves are seen coming off the vagi which lie next to the spinal cord, and finally branches either from the recurrent or from the lower limits of the vagi in the cardiac area are seen coursing toward the heart. These may be said to represent schematically the depressor nerves which carry the only sensory vagal fibers. Coming away from each sympathetic ganglion, we have represented other branches. In sequence from above downward these are called the superior, middle and inferior cardiac nerves. We have then to consider as possible nerves which should be cut in stopping the reference of stimuli from the heart to the central nervous system only the depressor nerves, which are of vagal origin, and the nerves from the heart which reach to the lower and middle cervical ganglia as well as to the first thoracic or stellate ganglion.

The original operation of Jonnesco included the removal of the cervical sympathetic ganglia on both sides from above downward, including the first thoracic ganglion. In view of our present knowledge, this would seem to remove all possible sensory lines of communication to the central nervous system except the depressor fibers. The proposal that the sensory impulses in angina pectoris might be carried to the central nervous system by the depressor nerve was made by Wenckebach, and certain surgeons have attempted to interrupt these lines of possible sensory communication. It is very doubtful whether the depressor nerve can be identified in an operative procedure. The only sure method of finding it would be to stimulate all fibers found in a certain region in the neck and study the effect upon the heart rate. This nerve is known by the anatomist to have a very variable course, and it is most unlikely that it could be identified with regularity in human cases. Furthermore, there is no reason to think that it carries stimuli which might result in the pain that occurs in angina pectoris. In the first place, stimulation of its central cut end does not produce the somatic reactions of rise in blood pressure and heart rate, sweating and emotional disturbances either in man or animal which one might expect if it could carry such impulses. In the next place, its point of central connection is in the region of the medulla and an overflow of stimuli here would hardly be recognized as pain in the brachial and thoracic region which is the usual location of the pain in the clinical disease, angina pectoris.

It is certain that if we consider angina pectoris as a cardiac disorder, we must imagine that the stimulus which ultimately results in pain arises in the heart. It is true that the pain in angina pectoris usually is present in the arm or upper thoracic region. This would seem to mean, if we accept the modern view of referred pain, as proposed by Head and Sherrington, that nonspecific impulses enter the spinal cord, and because of their intensity overflow and stimulate the sensory nerves in that region, so that in the case of angina pectoris the impulses must reach the spinal cord in either the lower cervical or the upper dorsal segments.

With this in view, let us turn to a review of what has happened to the patients who have been submitted to ablation of either the vagus or sympathetic pathways. For convenience of study we have divided them into the following five groups:

TABLE I.

GROUP I. The complete Jonnesco operation.
- A. Bilateral.
- B. Unilateral L or R.*

GROUP II. Operations upon the cervical sympathetic chain.
- A. Superior cervical ganglion procedures = either excision of ganglion or division of superior cardiac nerve, or A′ of the ramus communicans, that is, main connecting trunk.
- B. Middle cervical ganglion procedures = either excision of ganglion or division of middle cardiac nerve, or of the ramus communicans below ganglion.
- C. Inferior cervical ganglion procedures = either excision of ganglion or division of inferior cardiac nerve, or of the ramus communicans below ganglion.

GROUP III. Operations upon the depressor nerve.

GROUP IV. Combined operations, atypical, upon both the vagus and sympathetic elements.

GROUP V. Procedures aimed at the posterior nerve roots themselves.

*L or R = left or right sided.

Group I concerns the complete Jonnesco procedure, which consists in removal of the complete cervical chain down to and including the first thoracic ganglion. This group is subdivided into the classes in which the operation is completed on both sides or only upon one side.

Group II is that group into which we have arbitrarily placed all the partial cervical sympathetic procedures. These are further subdivided according to how much of the cervical sympathetic apparatus has been removed. There is the greatest variation in this group, but it is well to mention here that operation from the middle cervical ganglion down should have a quite different significance from those operations which concern solely the upper cervical ganglion and its ramifications. We have pointed out that the function of the upper ganglion is purely motor whereas we know sensory fibers run through the cervical sympathetic system, beginning as

high as the middle ganglion and including the first dorsal or stellate ganglion.

In Group III we have placed the various operations, unilateral or bilateral, upon the depressor nerve, and these constitute the only interference with the vagal system.

Group IV includes a few combined operations in which both the vagal fibers as well as the most varied group of sympathetic fibers have been divided.

Group V concerns procedures which attack the posterior sensory nerve roots. In some of these cases novocain or alcohol was injected into the dorsal ganglia; in others the roots were actually cut.

In Table II we have summarized the results in 120 cases selected from the literature. We have included in this analysis of the material available probably only a small fragment of the cases which have actually been performed. This is partly because certain of the data are so meagerly presented that they cannot be of value. Certain cases, in which it was obvious that the procedure was performed mistakenly for other diseases than angina pectoris, have been discarded. Certain authors, notably Leriche, who has stated that he has performed as many as 80 cases, have never presented their complete material in published form. Reasonable doubt can unquestionably be cast upon the final diagnosis in some of the cases used for this summary, and still further doubt may be cast upon the results as tabulated by the various surgeons. We have frequently found in articles that in summarizing his report the author has stated that all cases were relieved, and yet in the intimate case reports of the patients as appearing in the same article one finds such statements as, "the patient continues to take small amounts of nitroglycerin" or "the patient still complains of considerable retrosternal distress." In view of the fact that there may be a psychic element in the clinical disorder, angina pectoris, it is extremely hard to correctly classify the end results, for it is possible that quite unintentionally by holding out hope to the patient the surgeon may have done an amount of good which he has translated as an operative result. The material available, however, is sufficient to allow certain deductions to be drawn, and, although in reading the reports of cases one can never be absolutely sure that the patient submitted to operation had angina pectoris, it is most probable that the great majority of those included in this series actually suffered from this disorder.

A study of this material brings home the deep impression that it is unfortunate that surgeons should explore any fields in the diagnosis of which they may not be sufficiently expert. There is no diagnosis in medicine which requires greater discrimination than the diagnosis of angina pectoris. Since the cause of the disease is unknown, the clinical picture alone can be used in classifying

TABLE II.

Groups.	No. of cases.	Operative mortality.[1]	Result.[2]				Late mortality.
I. Jonnesco { A, Bilateral	9	0 = 0.0%	9 = G				2, 4 days, no pain
Jonnesco { B, Unilateral	18[3]	3 = 16.6%	8 = G	5 = I	2 = N.R.		1, 4 days
	27	3 = 11.1%	17 = G (62.9%)	5 = I (18.5%)	2 = N.R. (7.4%)		
II. Cervical sympathectomy A	29	2 = 6.9%	10 = G (34.4%)	11 = I (37.9%)	4 = N.R. (13.8%)	2 = ? (6.9%)	1, 2 months, 1, 8 days
" " A′	2	1 = 50.0%	1 = G				
" " B	3	.....		3 = I			
" " C	0						
" " A + B	4	.....	3 = G		1 = N.R.		
" " B + C	2	.....		2 = I			
" " A, B + C	13	1 = 7.6%	8 = G	3 = I	1 = N.R.		1, 2 weeks, 1, 13 days
	53	4 = 7.5%	22 = G (41.5%)	19 = I (35.8%)	6 = N.R. (11.2%)	2 = ? (3.8%)	
III. Depressor	12	.....	9 = G		2 = N.R.	1 = ?	1, 12 days, 1, 2 weeks, 1, 1½ years
IV. Combination II and III	2	.....		2 = I			1, 6 months, 1, 16 days
V. Posterior nerve root procedures	26	.....		26 = I(?)			
Totals	120	7 = 5.8%	48 = G (40.0%)	52 = I (43.3%)	10 = N.R. (8.3%)	3 = ? (2.5%)	

[1] Death first twenty-four hours postoperative.

[2] Arbitrarily classed as good (G), improved (I), not relieved (N.R.).

[3] One case by Tuffier in which the stellate and lower cervical ganglia were removed was placed in this group since the actual result approximates the effect of the complete Jonnesco procedure except innervation from the upper cervical ganglion which would remain unaffected.

cases. The clinical picture of angina pectoris closely simulates that presented by many cases of aortitis, of aneurysm of the aorta and of infarct of the heart. There may be those who believe that coronary disease is synonymous with angina pectoris, although there is plenty of evidence in cases which have come to autopsy, including the first case described by Heberden, that coronary disease may frequently be absent in patients suffering with the typical pain of angina pectoris, and in whom relief was given by the administration of nitrites.

The figures presented in Table II show that 62 per cent of the patients submitted to the Jonnesco procedure, both unilateral and bilateral, are in a satisfactory condition for a sufficiently long period after operation to justify the assumption that the operation has benefited the patient. In addition to this large percentage, 18.5 per cent have been improved. This means that 80 per cent of the patients submitted to this procedure have been improved. If we take the various procedures upon the cervical sympathetic chain as a whole, we find that 41.5 per cent of the patients are certainly relieved following the procedure and that an additional 35.8 per cent are improved. The total figures for Groups I and II show that roughly around 80 per cent in each group seem somewhat relieved. When one intimately surveys the individual cases in these two groups, it is obvious that *the results by the complete Jonnesco procedure are better than those given by the simpler procedures involved in any of the cervical sympathectomy operations.* The Jonnesco procedure, however, gives a slightly higher operative mortality. It is interesting to note that all the fatalities in this group occurred following the unilateral procedure, but this probably means that the patients who were not good risks found the one-sided procedure too great, and any patient who could survive the risk of operation—and this probably means the risk of any operation—would survive a second procedure on the opposite side.

In view of the discussion above concerning which pathways were interrupted in the various operations, it would be well to compare the figures for superior cervical sympathectomy with the other procedures, for in this operation we are concerned only with motor pathways. In operations involving the superior cervical ganglion or the superior cardiac nerve we find that only 34.5 per cent gave a good result, and that only 72 per cent were improved by the procedure. This does not contrast favorably with the results achieved by the Jonnesco procedure where 62 per cent were good results and 81 per cent were improved. *It appears from these figures that interrupting motor pathways is not so satisfactory a method of blocking the painful attacks in angina pectoris as interference with pathways which we know are sensory in function.* It is certain, however, that in some cases where the sensory pathways were blocked, and where only the superior cervical ganglion remained, that anginal attacks

have recurred with the radiation of pain into the face and neck, which is the area supplied by the superior cervical ganglion. This would indicate that the motor element is a factor in some cases of angina pectoris.

The operations in the depressor group are too few to draw any conclusions from, as are the combined operations in the depressor and cervical sympathetic group. Moreover, one can justly cast some doubt on the fact that the depressor nerve was actually cut in these procedures. If it was not cut the fact that some relief has been obtained gives us reason to again bring up the question as to how great the psychic element is in the clinical disorder, angina pectoris.

At this time we do not feel that it is justifiable to discuss procedures upon the posterior nerve roots. It seems possible that by destroying these roots, either with alcohol or by operative methods, the nervous arcs would be interrupted which allow the patient to perceive the symptom pain. The material presented, however, by those investigators interested in this procedure is not convincing. Certainly many of the patients did not suffer from angina pectoris, although there is no doubt that they had precordial pain. Again the relief is a temporary matter where novocain or alcohol is used, and, as a further consideration of this group, we feel that the injection of alcohol into the posterior nerve root, though possible, may not be such a safe procedure as its simplicity would seem to indicate. Things accomplished in surgery unaided by vision, or the use of a powerful drug like alcohol, and particularly when in proximity to the delicate structure of the nervous system, are often fraught with grave danger and entail serious consequences. The fact that relief can be obtained by such a method does not make us feel that this is the best way to obtain it.

Conclusions. It would seem that a sufficient number of cases have now been presented to draw certain deductions. From these figures it appears that operations which divide the known sensory pathways in the sympathetic nervous system connecting the heart with the central nervous system give a fairly high percentage of satisfactory results. It is apparent also that the complete Jonnesco procedure achieves part of its success because it interferes with a motor autonomic reflex as well as interrupts the sensory pathways. Whether this operation is unduly extensive, as proposed by Daniélopolu, and whether division of the sensory elements entering and leaving the two lower cervical and the first dorsal ganglia, but without removal of the ganglia, will yield more satisfactory results is still to be proven. The failure of any single procedure to alleviate the pain in all cases leaves us with the definite impression that much more is to be learned. If the division of a certain pathway eradicates the pain in one case, why should it not do the same in every case? The fact that it does not, and the fact that so many varied pro-

cedures give relief one time and again fail, arouses more strongly than ever our curiosity as to just what it is that results in the clinical picture, angina pectoris.

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CARCINOMA DEVELOPING IN THE PAROTID (STENSEN'S) DUCT.

With Clinicopathologic Report of a Case.

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The common pathologic conditions primarily affecting and involving the salivary ducts include the various types of infection, calculus formation and the lesions resulting from their association with each other. The usual complications and sequelæ of salivary concretions are obstruction, retention-cyst production and occasionally, following rupture of a sialocele, fistula formation. Chronic inflammatory changes, as a rule, are evident, and often are present to such a marked degree in both the duct and gland that the basic condition is masked beyond recognition. Secondary glandular enlargement, with accompanying pain, also may obscure the picture by diverting attention to the gland, instead of the duct.

Very little information is available concerning the neoplasms of the salivary ducts. The term "tumor" is often used in the sense of swelling resulting from stricture, obstruction, and inflammation, but references to "new growths" are very uncommon. From the occupational point of view, the pneumatoceles, occasionally formed in the parotid ducts of professional blowers, are interesting. Sénèque[1]

FIG. 1.—Dental roentgenogram showing shadows that were interpreted as representing areas of calcification in the nodule.

FIG. 2.—Photograph of sectioned specimen. Note tightly-fitting capsular structure about nodule. The mouth of the parotid duct is recognized by the attached tag of buccal mucosa. The hole in the center of the nodule is a needle puncture.

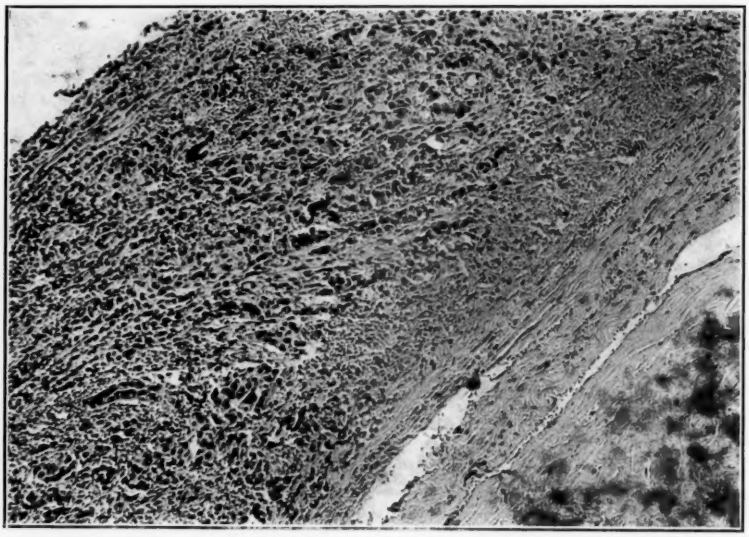

FIG. 3.—Low-power microphotograph (126 ×) showing cancer cells invading the soft tissues about the nodule. Note fibrohyaline nature of the nodule with numerous areas undergoing calcification.

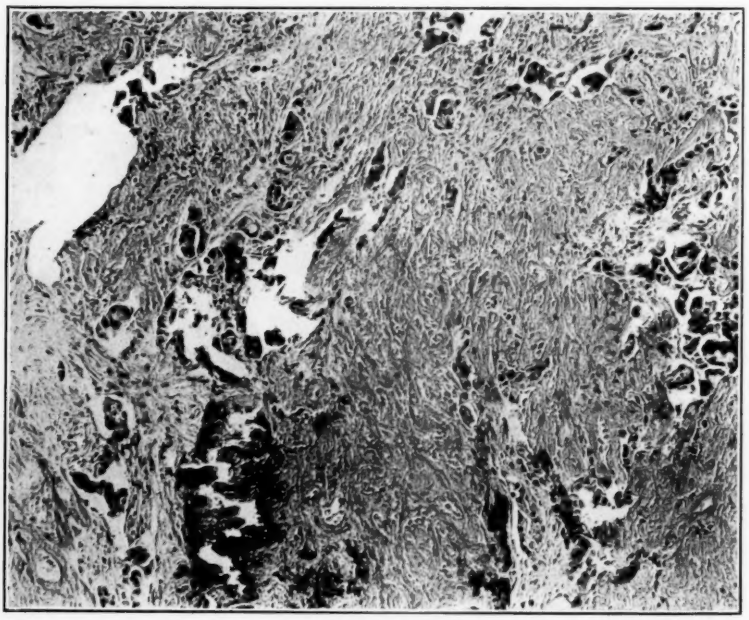

FIG. 4.—Low power view (126 ×) showing small nests of cancer cells that have invaded the fibrohyaline portions of the nodule. An area of calcification is present.

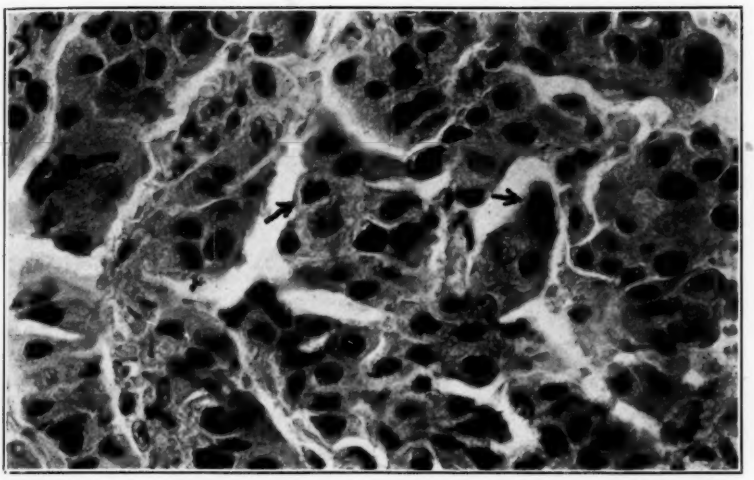

FIG. 5.—High-power microphotograph (460 ×) showing malignant, rapidly-growing, anaplastic, squamous epithelial cells; the arrows point to cell-division stages.

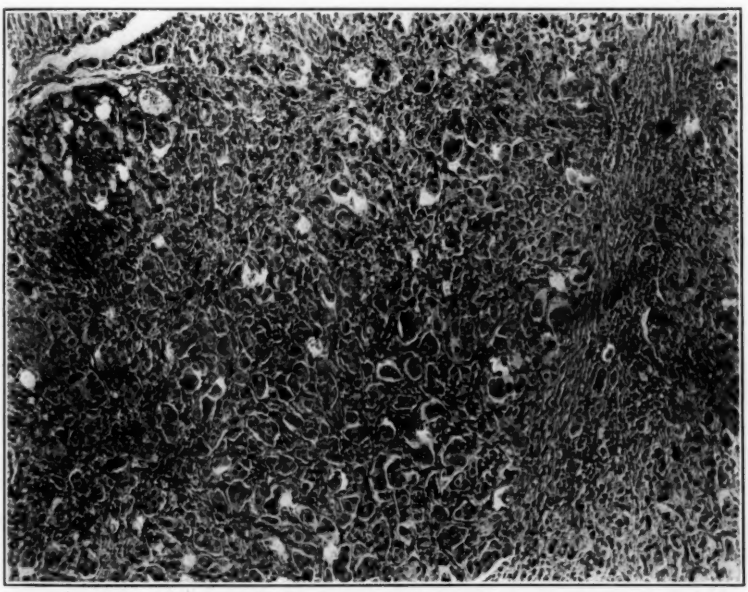

FIG. 6.—Low power view (126 ×) showing metastasis to cervical lymph node. The structure is a reduplication of that noted in the primary growth.

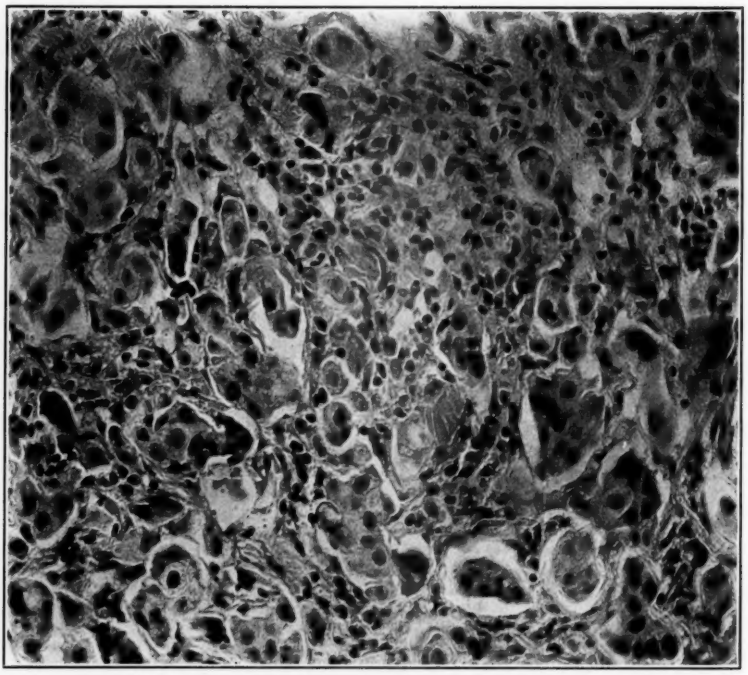

FIG. 7.—High-power view (276 ×) of metastasis to cervical lymph node. The cells are quite similar to those composing the primary growth.

reports such a case with an associated multilocular retention-cyst occurring in a glassblower, and refers to other similar cases. A search through the scanty literature on the subject indicates that instances of malignancy occurring in a duct, either primarily, or in association with salivary concretions, are quite rare. Harrison,[2] in a recent contribution, finds that 375 cases of salivary calculi have been recorded since 1825; there is no mention of malignant disease occurring in connection with, or as a sequel to, sialolithiasis in any of these cases.

The following case* of malignancy developing in the parotid duct in connection with a peculiar calculus-like structure, and terminating fatally, exhibited such unusual features that it is placed on record because of its clinical and pathologic interest.

Case Report.—C. H. (P. G. H. Surg. Path., No. 6670), a white female, aged sixty years, came to the radiologic clinic of the Philadelphia General Hospital, in the service of Dr. John B. Carnett, complaining of pain in the left side of the face. In February, 1925, she had first noticed a small lump behind the lobe of the left ear. Soon after this she experienced periodic attacks of dull, aching pain in the left cheek and which often included the forehead, scalp and ala nasi. These attacks became more frequent, and soon were so severe that she could not sleep. In August, the left side of the face suddenly became swollen, the eyelids drooped, there was much lacrimation, and fluid ran out of the left corner of the mouth when she drank. She stated that for many years there had been a "small lump" inside the left cheek; at about this time this lump began to grow larger "because of irritation caused by her false teeth." Previously, the lump had never been painful, or varied in size. She had never noticed a discharge of any kind from the duct, and the parotid gland had never been swollen or tender. In September 1925, the nodule back of the angle of the left jaw was removed for diagnosis. It proved to be an enlarged cervical lymph node, showing metastatic carcinoma. Dr. E. A. Case, of the Polyclinic Hospital, gave the microscopic diagnosis of "scirrhus carcinoma" (Figs. 6 and 7). Shortly after this the patient came to the Philadelphia General Hospital for relief of pain, and treatment. She had lost 25 pounds in weight during the past eight months.

On physical examination, there was complete left facial paralysis, and the cheek was swollen and puffy. Inside the cheek, in the region of the distal portion of the parotid duct, and about 1 cm. from its mouth, a small, firm, spherical nodule, apparently about 1 cm. in diameter, was felt. This nodule was fixed to the tissues, and was not tender on palpation. Cyst formation or glandular enlargement was not demonstrable. There was no ulceration or induration of the buccal mucosa. A roentgenogram of the nodule revealed a shadow suggestive of calculus or tissue undergoing calcification (Fig. 1). The remaining physical findings were irrelevant. The laboratory examinations were negative, except that the red blood cell count was 3,800,000.

October 8, 1925, under local anesthesia, Dr. Carnett excised a small, apparently encapsulated, whitish, calcific nodule from the distal portion of the parotid duct. The patient was discharged October 21, with the facial condition improved. She was readmitted December 23, because of severe and frequent pains in the left half of the head. Despite numerous applications of radium, she gradually failed and became cachectic. Local

* I am indebted to Dr. John B. Carnett, of Philadelphia, for the use of the clinical data in this case.

recurrence was never demonstrable, but there were clinical evidences of metastasis. Exitus occurred in June, 1926. Necropsy was not permitted.

Pathologic Study. The excised mass consisted of a firm, rounded, calcific structure, surrounded by a tightly fitting capsule. A tag of buccal mucosa was attached. The nodule was sectionable (Fig. 2); the cut surface was grayish-white, and the tumor appeared to be composed of dense fibrohyaline tissue, throughout which were scattered many calcified areas. The attached tissues were infiltrated, and fixed to the nodule; malignancy was not suspected. Grossly the specimen was regarded as an atypical salivary calculus about which an extensive chronic inflammatory reaction had occurred.

Microscopically, an anaplastic or undifferentiated squamous-cell carcinoma was seen growing around, and into, the nodule (Figs. 3 and 4). The nodule itself was composed of very dense fibrohyaline tissue, throughout which many foci of calcification were demonstrable. It did not have the structure of a true calcific salivary concretion. The cancer cells were large and spheroidal in shape; the nuclei were large, vesicular, and deeply stained; the nucleoli were enlarged and prominent. Numerous mitotic figures were seen (Fig. 5). Prickles and pearly bodies were not demonstrable. Small nests and cords of cells invaded the neighboring tissues, and occasionally the nodule proper (Fig. 4) without recognizable structure formation. Histologically these cancer cells resembled modified, immature, squamous epithelial cells.

Sections prepared from the cervical lymph node metastasis (Figs. 6 and 7) revealed a secondary neoplastic growth composed of cells, very similar in appearance to those of the primary tumor.

Dr. James Ewing, of New York, in confirming our diagnosis, stated that he had never seen a carcinoma develop from, or in association with, a calculus in Stensen's duct.

Comment. The possible etiologic relationship of cancer to lithiasis is generally recognized, and, in the light of available data seems fairly definitely established in certain organs. Instances of carcinoma of the biliary tract associated with biliary calculi are well known. Ewing,[3] in reviewing the literature on the subject, found that gall stones were present in 69 to 100 per cent of the cases of gall bladder cancer studied, and that the proportion of cases of cholelithiasis which develop cancer is estimated from 4 to 18 per cent. Slade's[4] study also indicates that the two occur together in a high percentage of cases; he found that the calculi were usually rough when associated with cancer, and concluded that gall stones might be looked upon as a determining cause of gall bladder malignancy.

Carcinoma of the urinary tract associated with urinary calculi is less frequently seen. Coryell[5] reported 9 cases of concomitant renal cancer and stone, and Menétrier and Martinez[6] describe in detail a case they have observed in which it was shown that the stone actually prepared the ground for the development of cancer by chronic irritation of the epithelium. We have been unable to find any recorded instances of ureteral or urinary bladder cancer associated with ureteral or vesical calculi. Boyd[7] states that no relationship has ever been shown to exist between carcinoma of the bladder and stone.

Minet's[8] case of pancreatic malignancy, occurring with pancreatic lithiasis is unusual and interesting.

Salivary calculi are relatively common, yet infrequent compared to the incidence of biliary and urinary calculi. Edington[9] reports 9 cases of salivary lithiasis, 8 occurring in the submaxillary duct, and one in the parotid duct. In no instance were the sequelæ and complications other than obstruction, enlargement of the respective gland, and secondary infection. Bailey[10] refers to the 20 cases of cancer of the submaxillary gland on record, and states that "there is very little evidence to show that calculi predispose to this condition."

The relatively high frequency of carcinoma of the gall bladder occurring in association with cholelithiasis, as compared with the rather low incidence of associated urinary tract malignancy and calculi, and the extreme rareness of concomitant salivary duct malignancy and stone may be due to several factors. According to Wells[11] the majority of gall stones are composed chiefly of cholesterol, in combination with the calcium salts of bile pigment, and small amounts of organic and inorganic material. The rough, rounded crystalline stones often contain over 90 per cent of cholesterol. Urinary calculi vary considerably in composition, but consist mainly of urates, oxalates, carbonates, and phosphates in combination with calcium, ammonium and magnesium. Pure uric acid and calcium oxalate stones are occasionally met with in acid urine; in the presence of infection, phosphates and urates are deposited. Pancreatic stones consist almost wholly of calcium carbonate; varying amounts of calcium phosphate and magnesium carbonate are occasionally present.

Salivary calculi are rather similar to pancreatic stones, and are composed chiefly of calcium carbonate and phosphate, in combination with traces of organic matter. Pathologic deposition of calcium salts in diseased tissues occurs ordinarily in the ratio of six parts of calcium phosphate to one part of calcium carbonate; traces of magnesium phosphate may be present.

Infection and inflammation sooner or later supervene on lithiasis in the majority of cases. Coincident with this the blood calcium rises, and there follows, as a rule, deposition of calcium salts over concretions which were originally of pure and specific composition.

When these data are analyzed and are balanced against the clinical and pathologic findings as regards tissue changes due to lithiasis, it appears that cholesterol is the only constituent of calculi that possesses possible carcinogenic properties. Excepting certain apparently harmless elements found mainly in urinary stones, the remaining ordinary components of calculi are common to practically all calculi, and pathologic processes where calcification occurs. Roffo[12] has found a high percentage of cholesterol in early and well-developed cancerous lesions, with associated hypercholesterolemia

He concludes that cholesterol is involved with the enhanced nutritional function of tissue growth as known in neoplasia, and that it may act as a precursory agent in the development of malignant disease. The cholesterol metabolism in malignancy, and its specific effect on tissue proliferation remain subjects for further investigation, but from the striking relationship that exists between gall stones and gall bladder cancer, the possibility of cholesterol playing an important, and perhaps etiologic, rôle in the development and behavior of certain types of cancer is strongly suggested.

The constant irritation of the epithelial cells of the mucosa by calculi, particularly in the presence of infection, is an illustration *par excellence* of the view commonly held that chronic irritation is a prominent factor in inducing malignant transformation of the epithelium. Yet, on analysis, one is struck by the relative rareness of associated stone and cancer in all organs except the gall bladder. The gall bladder is lined by tall, columnar, mucus-secreting cells; in practically every other organ which is the seat of calculi, the lining mucosa is of the squamous-cell or transitional-cell type. This might suggest that glandular mucosa is more susceptible to malignant transformation than squamous mucosa under the influence of chronic irritation, but until the effect of cholesterol is determined such a conclusion is not justifiable. Infection, inflammation, and irritation bring about changes in the mucosa which in time are recognized as hypertrophy, and occasionally, metaplasia of the epithelium, with attendant surrounding fibrosis. That a process which is essentially protective and defensive in its reaction to harmful agents should, through overstimulation, become self-destructive, seems unnatural, yet there is evidence that, following metaplasia of epithelium, there ensues an actual malignant transformation of the changed cells in rare cases. We believe our case to be an example of this.

There are certain peculiarities about our case. The nodule, although largely calcified, cannot be regarded as a true calcific salivary concretion because of its histologic appearance. Basically it appears to have been a fibrous structure that in time became hyalinized and partly calcified. Its location and long period of duration probably caused it to act very much like a sialolith, however, causing partial obstruction. One is tempted to explain matters on the supposition that the structure, whatever its true nature, over a long period of time brought about, possibly through mild continuous irritative activity, a change or metaplasia in the short columnar cells that normally line the parotid duct, which, in turn, eventuated into malignant transformation of these cells. This conception fits both the histologic picture and the clinical course of the case. The cancer cells were anaplastic and appeared to be growing rapidly, microscopically. Clinically metastasis occurred relatively early and a fatal termination came soon. In addition to its clinical and pathologic interest, the case is worthy of record in that it designates the parotid duct as a rare source of carcinoma of the cheek.

Summary. 1. An instance of carcinoma developing in the parotid duct in association with a peculiar, calculus-like structure, is recorded.

2. The etiologic relationship of lithiasis to malignancy is reviewed. Associated stone and cancer are well known in the biliary tract. In all other organs where calculi occur, carcinoma seldom supervenes on lithiasis. In the salivary system, associated stone and cancer are practically unknown.

3. It is suggested that cholesterol plays an important rôle in the development of gall bladder cancer. Chronic irritation, secondary infection, and inflammation bring about hypertrophic and proliferative changes in the mucosal epithelium, but do not appear to be carcinogenic *per se*. Several factors appear to be operative in inducing the malignant transformation of epithelium in the presence of calculi.

4. Metaplasia of epithelium occurs rarely as an atypical reaction to long-continued irritation. Malignant transformation of the changed epithelium may follow this.

5. Our case designates the parotid duct as a rare source of carcinoma of the cheek.

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THE MEDICAL TREATMENT OF ULCER OF THE STOMACH.*

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The treatment of gastric ulcer is a less congenial subject to the physician than the treatment of duodenal ulcer, because the former

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is usually a more serious condition and the results of medical treatment less striking. In fact, we occasionally meet the opinion that there is no medical treatment of gastric ulcer; that the patient should go at once to a surgeon when this diagnosis is made. With this, our own experience does not agree. We will give our observations in a series of 51 cases in private practice in which this diagnosis has been made, and which have been followed for five years or more, giving the details of the medical treatment used and the end results which have been obtained.

The Accuracy of Modern Diagnosis. Accurate diagnosis is essential to good treatment. In the past the surgeon had a great advantage over the physician; usually he knew when he was treating gastric ulcer, because he had seen and felt it, and the physician had not. Many ulcers were overlooked by the physician and called "hyperacidity," and many so-called ulcers were given medical treatment, and included in medical statistics which were not ulcers at all, but neuroses, pathologic gall bladders, or appendices; in addition it was often not possible to make a definite distinction between gastric and duodenal ulcers. This led to a sharp contrast between medical and surgical statistics.

Our present-day accuracy of diagnosis of gastric ulcer without operation is over 90 per cent. It is rare in a carefully studied case either to overlook an ulcer, or to diagnose ulcer when it is not present. This is largely due to the addition of the Roentgen ray to our other methods. The Roentgen ray not only discovers the deformity of ulcer, but locates it in the stomach or duodenum, gives us an idea of the size of lesser curvature ulcers, and by the Graham test and in other ways detects many pathologic gall bladders simulating ulcer. It may also discover chronic changes in the appendix. On this basis, a new set of medical ulcer statistics have been accumulating in the last ten years, which have real value.

Some difficulties in diagnosis still are met. The cases with gastric hemorrhage with few or no digestive symptoms and negative Roentgen ray findings are hard to classify. An occasional pyloric cancer is hard to distinguish from pyloric ulcer at the first examination, but is almost always discovered when followed with painstaking care for a short time.

The accuracy of modern diagnosis brings with it the responsibility for earlier and better treatment. The long medical histories with years of medical treatment are a reproach. Many ulcers in private practice have gone unrecognized for years because they were not taken seriously enough, and no Roentgen ray examination made. It is safe to say that fully one-half the gastric ulcers have been diagnosed late.

It is important for the present-day practitioner to have the *early* ulcer picture in mind, the common hunger pain or "hyperacidity" syndrome, the relief by food and by alkalies, and the

Roentgen ray deformity, and not to think of severe pain, hemorrhage, anemia, obstruction and perforation as the cardinal symptoms.

By using the Roentgen ray promptly we can often make an earlier diagnosis when the patient is younger, when remissions are long and there are no complications. This has an important effect on treatment. We are not asking impossibilities; early cancer diagnosis is very hard; early ulcer diagnosis is not.

The Selection of Cases for Medical Treatment. We think first of the absence of complications, such as bleeding, obstruction, and, of course, perforation. We will take up later the limits of medical treatment in bleeding and obstructive cases. Gastric ulcers are less favorable than duodenal, not so much on account of the cancer risk, but because they do not give as good results under medical treatment. We must also give medical treatment to many patients because they prefer it if it can be made successful, and to some others because of lesions outside the digestive tract which make operation dangerous.

In selecting patients for medical treatment I wish to especially emphasize that the younger ones do better. We get a decidedly higher percentage of cures in patients under forty-five years than over. The most favorable cases are those which have short histories, short attacks and long remissions (the so-called acute recurrent type of ulcer) and those who are intelligent and are willing to see the doctor occasionally during a period of several years, even when symptom-free. We can make medical treatment a success with a larger proportion of private than hospital patients, because of their greater intelligence, easier circumstances, better food and better contact with the physician.

We used to think that the discovery of an hour-glass stomach was an indication for operation. We now realize that this is true only when it causes symptoms. We have several cases who have been under occasional observation for years, who have no obstruction, and enjoy excellent health, and would not consider an operation. Dr. F. H. Lahey, of Boston, has reported the same experience.

The General Treatment. The plan of medical treatment must be simple, logical and above all practicable. Most people cannot afford to "make a pet" of an ulcer, as Dr. Mayo says, or to devote much time and money to repeated hospital treatment.

We like to classify and plan separately for gastric and for duodenal ulcer. The treatment is very similar, but the medical responsibility, the follow-up, the results and the surgical aspects differ somewhat.

Our treatment is still largely symptomatic, since the cause is not definitely known, but evidently the mixed result of chemical, mechanical, infectious and nervous factors. Vague talk about diatheses gives no practical help at present. We will sum up briefly

the chief factors in medical treatment in the approximate order of importance.

A *bland diet* is essential and easily understood. The Leube and Lenhartz and Sippy diet use much the same foods. We need ride no hobbies, but consult the taste of our patient. Milk and egg, milk and cream or cereal gruels at the start do equally well.

Frequent feeding is the great thing, and must be emphasized, six times a day or even more at the beginning. This is easily arranged with ambulatory cases by means of a thermos bottle. We have given up the use of duodenal feeding in ulcer as it is less comfortable for the patient and has no real advantages over mouth feeding.

These are the two routine diets which we use, which allow sufficient choice of food to suit individual tastes. The "periods" in Diet I are approximately a week, but are varied to suit the severity of the case. The strict Lenhartz régime of egg and milk, only in the first week is distasteful to some people. We prefer to vary it with gruels and milk and cream.

Diet I. *First Period.* Strained cereal gruels or strained cream soups made from vegetables (such as potato, celery, corn, asparagus) or milk and cream; equal parts are given in one- or two-hourly feedings, beginning with 1 ounce and increasing up to 3 or 4 ounces. If desired, the Lenhartz feeding may be given, namely, 8 ounces of milk and 2 eggs beaten up and divided into twelve feedings, one every hour. Each day add 1 more egg and 3 ounces of milk until 6 eggs and 1 quart of milk are taken. On the third day add ½ ounce of sugar or milk sugar to the beaten eggs, gradually increasing to 1 ounce of sugar.

Second Period. Two or 3 eggs, soft cooked; three feedings of 1 ounce each of boiled rice, or other well-cooked cereal (not oatmeal) served with sugar and cream. One-half to 1 ounce of butter per day. Gruels, cream soups, milk, egg and milk, 1 or 2 pieces of very dry toast, well chewed, or milk toast, plain crackers, macaroni, Mellen's Food, or malted milk, junket, custard, cream toast, ice cream. Six meals a day.

Third Period. Add 1 or 2 ounces of tender beef, chicken, chop or steak, daily; also simple cornstarch, custard and rice puddings.

Fourth Period. Add well-cooked mashed potato or squash, vegetable purées, finely chopped spinach; apple sauce or stewed pear.

General Directions. Eat slowly, chew well; no very hot or very cold foods; no worry at meals. Never eat until overfilled. Take a little lunch between meals, for example, a glass of milk, malted milk or cocoa, with 1 or 2 crackers. No raw fruit or vegetables for six months.

Diet II. The general plan of the diet is three moderate-sized meals at regular intervals in the day, and supplemental meals of malted milk or milk reinforced with cream, cocoa and crackers between meals and before retiring. All of the solid foods should be tender,

cut very fine on the plate and thoroughly masticated before swallowing. Altogether, foods should be taken at least five or six times a day in one or the other of the two types of meals. No meat broths, condiments, spices, coffee, "soda water," alcohol, coarse or salted food, very hot or very cold foods.

The foods permitted for the main meals are as follows: Cream soups, eggs, soft cooked (2 to 4 in a day), cereals (well-cooked) with cream in the morning, rice, macaroni, well-cooked and mashed potato or squash, vegetable purées, finely chopped spinach (no green vegetables, raw fruits, berries or nuts). Desserts, any made of milk, eggs and cereals (custards, simple puddings) and jellies, cream cheese, cooked fruit—apple, pear, peach, prunes. The best drink at the meals is water, hot cocoa, or malted milk. Butter, cream, milk, eggs, cereals and bread remain the main foods of the diet. Olive oil may be taken after the main meals, a dessertspoonful or tablespoonful.

After the first or second week fresh beef, lamb or chicken, roasted or broiled, or fresh fish, broiled, baked or boiled, may be taken once a day (no mackerel or salmon).

Rest is important. In most cases of gastric ulcer a week or two in bed at the beginning of the treatment is desirable. Some need twice this time, and some milder cases give good results with ambulatory treatment (a large percentage of our duodenal cases do well on ambulatory treatment). It is usually easier to arrange diagnostic tests and to begin systematic treatment in a hospital rather than at home.

Drugs. We do not use many; even alkalies are not essential and can be omitted in many bed cases with good results. They are very useful; however, they simplify treatment, especially at first. We use them regularly in the form of the familiar Sippy powders (No. 1.—Sodii bicarb., magnesii oxid. pond. āā, ℥j; No. 2.—Sodii bicarb, ℥iij and calcii carbonat., ℥j), given alternately in 20 to 30 gr. doses midway between feedings, beginning with four to six times a day and usually dropping to two or three times a day in a week or two. No. 1 powder may have to be reduced or replaced by No. 2 if it is too laxative. Magnesium oxide is used in amount large enough to give one daily formed stool, the rest of the alkali being given as sodium bicarbonate and calcium carbonate. The use of two or three powders a day midway between feedings is best continued for several months, after that we often omit the routine use of powders and depend chiefly on the diet and hygienic measures, using the alkalies only occasionally. Some patients take one to three powders a day, for six to twelve months.

An excess of alkali may cause gastric irritation or even an actual toxemia with renal changes which has been described by Hardt and Rivers, and is characterized by dizziness, headache, nausea and vomiting and important changes in the blood chemistry. They

found it in 30 per cent of a series of thirty ulcers on the Sippy treatment. It cleared up in one or two days on stopping the alkalies. They consider that alkaline therapy directed to complete neutralization of gastric acidity may be harmful. Dr. S. M. Jordon, of the Lahey Clinic, of Boston, found alkalosis in only 3 per cent of a series of 100 carefully studied cases of ulcer on the Sippy régime. We have found gastric irritation very rare with our moderate use of alkalies, and actual alkalosis even more rare. We have seen it in only a small fraction of the cases with pyloric obstruction, and will take it up more fully under that heading.

The "hunger pain" of ulcer is the result of many factors, such as food irritation, hyperacidity, pyloric spasm, hyperperistalsis, hunger contractions and hyperesthesia. Alkalies are especially useful when the pain is accompanied by gastric distention, as in addition to neutralizing acid; they help partly by causing belching of gas and by relaxing the pylorus.

Atropin is useful to relax spasm, quiet peristalsis and check true hypersecretion. Rather large doses are usually needed $\frac{1}{100}$ to $\frac{1}{50}$ gr. ($\frac{1}{2}$ to 1 mg.) of atropin sulphate, given by mouth, once or twice a day. It helps to carry the patient through the night, which is much the longest interval between feedings, and avoid "night pain" at 1 to 3 A.M.

Bismuth salts have a remarkable quality of covering a large surface of mucous membrane and have some value as a protective in ulcer, but we do not use them much because the diet in the early weeks is very bland and apt to be constipating.

Tobacco is important and unfortunately often allowed. Many proved cases of ulcer come to me smoking ten to twenty cigarettes or four or five cigars a day. It has an important effect in stimulating spasm and gastric secretion; it antagonizes the rest of the treatment and should be cut very low or omitted for some months at least.

It is important to remove infection in the remission period, such as septic teeth, tonsils, sinuses, and so forth. If the appendix or gall gladder are involved this puts the patient in the major surgical group.

Treatment in Remissions. This is a crucial point in medical treatment which is often neglected. Relief of pain is not a cure. It is usually easy to stop a recurrent attack in ulcer, to relieve pain, check vomiting and make the patient comfortable within a short time, usually in a few days. Our difficulties begin when the patient is symptom free. At first he is anxious, perhaps frightened, when the diagnosis of ulcer is made, and is very willing to coöperate; later the fear of the disease wears off when he finds himself promptly relieved and feeling entirely well. Both patient and doctor may get too lax, the diet is increased too rapidly, tobacco may be abused, the patient is too active physically, he gets tired, a little infection

may appear in the fall or spring and we have a recurrence of the ulcer.

This sort of thing is the bane of medical treatment, which should be well ordered and progressive, like that of diabetes. A foolish diabetic does not keep well, neither does a foolish ulcer patient; we may go a step further and say to the doctor, that an ulcer which is foolishly treated does not get well. The symptom-free ulcer patient is like the sugar-free diabetic—he is in a happy condition, which must be continued even at some sacrifice. The treatment is not really irksome, the restrictions are mild compared to those in diabetes, but they must be followed to get a permanent cure.

Almost any doctor can stop an attack; it is what we do in remissions which count the most—in educating the patient, in rooting out infections and preventing recurrence. We ought to explain to the patient at the start the importance and chronic nature of the disease, the tendency to recurrence and the duration of some supervision for at least two years. Much medical treatment still lacks a logical plan and is not systematic and thorough enough to get good results. If we recognize our shortcomings we can soon end them.

Follow-up System. A good follow-up system is vital in ulcer, just as in diabetes. We need occasional office reports, occasional examination of the stool for blood, occasional later examinations of the stomach with the Roentgen ray. It is never fair to let the patient shift for himself and try his luck on the wrong food.

A late follow-up of these patients for three to five years or more is also of great value in getting real end results of treatment, which are often neglected. I am suspicious of some of the medical statistics of "cures" in ulcer and feel like asking how long the cases have been followed up. The figures for so-called "cures" are distinctly higher in the first year or two after treatment is begun, than in three to five years or more; often 10 or 15 per cent must be taken off the early high figures of the patients who are well.

Use of Roentgen Ray and Occult Blood Tests to Follow the Results of Medical Treatment. In judging the results of medical treatment, we depend largely on changes in the patient's symptoms and signs (disappearance of hunger pain and distress, vomiting, gross bleeding, weight changes, tenderness and so forth), but in many cases we may get valuable help from blood tests and from the Roentgen ray.

Testing the feces for blood is an important routine. A meat-free diet must be used, and low intestinal bleeding excluded. Meat is not usually added to the routine ulcer diet until the third or fourth week, so there is no interference with early blood tests of the stools. Positive occult blood tests showing an active ulcer or recent hemorrhage usually entirely disappear in five to seven days under medical treatment. Any delay in the disappearance of blood is important and must be explained. It may be due to an ulcer which is not controlled by medical treatment and continues to bleed, or to a

cancerous ulceration; in both cases surgery must be considered promptly.

The Roentgen ray not only gives us the size and position of the ulcer, but enables us in a large degree to follow the course of healing. It is important to know just what a gastric ulcer is doing under medical treatment. We find that the peristalsis becomes less active and more normal, pyloric spasm lessens, the stomach empties better and above all the local deformity of the ulcer disappears, the crater fills up and the edges smooth out often in from one to four weeks. This is best seen in a lesser curvature ulcer, where we have it in profile (Figs. 1 to 6). In pyloric ulcer some local deformity due to spasm or scar tissue is often very persistent.

It is needless to say that these changes must be carefully correlated with changes in symptoms and other physical signs. Occasionally the Roentgen ray signs may be more important than the clinical. The patient may lose his symptoms and gain weight, but lack of healing shown by the Roentgen ray may give the best indication of a severe lesion. The best time for this reëxamination of the stomach is at the end of one or two weeks after treatment had been begun, again after one or two months, and at some later period.

There is some objection to Roentgen ray studies of local deformity as an index of the healing of an ulcer. The crater may fill with food or mucus and appear healed, or the stomach be rotated a little at subsequent examinations and the ulcer hidden. These objections call for careful work and interpretation, but are not serious. This Roentgen ray evidence of the rapid healing of gastric ulcer has been checked up by operation in several of our cases and found to be an actual fact.

This Roentgen ray study, together with the examination of resected material, has taught us much of the life history of ulcer—the time taken to form and heal at different stages and the degree of healing in intermissions. The discovery, that good-sized lesser curvature ulcers will disappear almost completely within four to six weeks, has been a surprise.

Late Results of Medical Treatment in Private Practice. The material is as follows: Of 51 gastric ulcers, 9 were operated upon at once and 41 put on medical treatment and tabulated below; 135 duodenal ulcers who were put on medical treatment are listed for comparison. These patients have been thoroughly studied by modern methods, and we have every reason to believe that 90 to 95 per cent at least were actual ulcers. They have been followed for three to five years or more to get actual late results. This is essential in this chronic disease when remissions and recurrences are so characteristic. Doubtful cases and short follow-ups have been excluded.

TABLE I. RESULTS OF MEDICAL TREATMENT.

	Gastric ulcer, 41 cases, per cent.	Duodenal ulcer, 135 cases, per cent.
Well	39.0	59.2
Better	29.0	22.2
No better	2.5	4.5
Later operation, after medical treatment	24.5	14.1
Died under medical treatment	5.0	0

You will note that more than one-third of the gastric ulcers are well, less than one-third better and about one-fourth were operated upon after unsuccessful medical treatment. Among the well cases the duodenal ulcers easily lead.

If our per cent of well cases under medical treatment, 39 per cent gastric ulcer and 59.2 per cent duodenal, seems moderate in comparison with some other medical figures, remember that the patients have been followed for three to five years, and that figures showing apparent cure will be 10 to 15 per cent higher at the end of only six months or a year, because some of these cases recur later. If these figures seem high to some surgeons, remember that the cases include many of the earlier, milder type of ulcer, and that painstaking care has been taken in the medical treatment in periods of remission, in educating the patient as in diabetes. Some cases listed as better, but not well, would no doubt be better still with an operation, but the patient often refuses if he is almost well or the intermissions are long. Nearly twice as many gastric as duodenal ulcers were operated upon after unsuccessful medical treatment.

There were no deaths among our duodenal ulcers under medical treatment. The 2 cases (5 per cent) of gastric ulcer died, 1 of cancer, apparently developing in a large inoperable ulcer in an elderly man with a bad heart, and 1 of a complicating diverticulitis of the sigmoid.

In looking over ulcer statistics we must always note what group is studied, whether a selected severe group sent to a great surgical clinic, or an average or milder group sent to a medical man in hope of medical relief. Our medical statistics give a general impression, but not mathematical accuracy, because patients occasionally change from one group to another, and while averages are interesting, the prognosis of the individual case may be different, either above or below the average.

The Advantages, Limitations and Risks of Medical Treatment. The advantages of medical treatment are that most patients prefer it. There is no mortality from the treatment itself, and nearly 40 per cent of gastric ulcers, and nearly 60 per cent of duodenal ulcers, get well and stay well, even if followed for a long period.

The disadvantages are that it is more tedious, requires more self

control (like diabetes), and an unintelligent or poor patient may find it difficult to carry out, and allied pathology in the abdomen may not be discovered and removed at the start.

There is some overlapping of medical and surgical treatment. There are cases which are best treated medically, and others best treated surgically, but there are some which may be treated in either way. The treatment sometimes depends on the clinic to which the patient goes. The patient with moderate grade spastic pyloric obstruction going to Sippy's Clinic some years ago would have undoubtedly had medical treatment, the same patient going to a surgical clinic would undoubtedly have had a gastroenterostomy.

It is unwise to have medical and surgical treatment overlap too much. It is unwise for the physician to keep cases of pyloric obstruction too long on medical treatment in the hope that pyloric spasm will entirely disappear. It is unwise for the young surgeon to operate upon many uncomplicated duodenal ulcers in young persons with long remissions, who could easily be cured by medical means. The patient has a right to expect the kind of prompt and efficient treatment which is simplest and will suit him best. The doctor does not always make the decision. There are illogic reactions to operation on the patient's part. We have the recurrent bleeding or very obstructing ulcer who refuses operation, and the young neurotic uncomplicated case who "would like to try a gastroenterostomy."

The Ulcer-cancer Question. The possible development of cancer on the base or border of a chronic gastric ulcer has an important bearing on the treatment, and is a difficult subject to discuss because there has been so little agreement among pathologists about it. We will quote only a few typical figures which vary from 71 per cent (McCarthy), 21 per cent (Finsterer) to 5 per cent (Ewing), with many other pathologists near the lower figures (Aschoff, rare; Crile, probably less than 5 per cent; and so forth).

Each man is impressed by his own experience and that in his own locality. Ours all points one way. In our series there was only 1 case in 51 gastric ulcers, about 2 per cent. At the Peter Bent Brigham Hospital, in Boston, they record 4.5 per cent in 201 cases. At the Massachusetts General Hospital Dr. Wright, the pathologist, says: "Cancer developing on chronic ulcer of the stomach is very rare, that is, cancer found in only one portion of a chronic ulcer. I have seen only a few, perhaps 3 or 4 cases, in my life."

Dr. F. B. Mallory, the pathologist at the Boston City Hospital, says: "We have ulcerating cancers, but I have never seen a cancer originating in peptic ulcer, that is, a chronic ulcer with cancer nests in the border or base."

A number of excellent clinicians who have treated many cases of ulcer of the stomach are not sure that a single case treated in their

clinics has later developed cancer, and others a possible 1 to 5 per cent. Einhorn, Rehfuss, Smithies, Soper, Friedenwald, Alvarez, Richard Cabot and Harlow Brooks place the figure variously at 0 to 1 or 2 or 5 per cent. These reports of cases having prolonged medical treatment would be just the ones to show cancer development if such a change occurred. If there were 70 per cent of cancers lurking in the background we should be swamped with them.

The willingness of the surgeon to do a gastroenterostomy in gastric ulcer throws light on his opinion of the importance and frequency of cancer development. Gastroenterostomy with its lower mortality was the operation done in nearly one-half our gastric ulcer series without later development of a single cancer as far as we know.

One is left with the impression that nearly all cancers supposed to develop from chronic ulcer have been malignant from the start.

There is no doubt that a large number of gastric ulcers are best treated surgically. In our series of 51 cases 9 were operated upon at once and 10 more were operated upon later after medical treatment, making 37.2 per cent in all. There is also no doubt that a considerable number, 39 per cent in our medical series, get a satisfactory result from medical treatment without taking undue risk. It certainly is not necessary to treat gastric ulcers with the idea that a large number will turn to cancer, for if this is done the cases lost at operation might easily be greater than the cases lost by cancer.

We started our medical treatment of gastric ulcer with a healthy fear of the possibilities of cancer, but were encouraged by the present opportunities to see what is happening to the ulcer by means of the Roentgen ray and by the rapid disappearance of many gastric ulcers under medical treatment in four to six weeks, and by finding that cancer developing on our gastric ulcers was a rarity (approximately 2 per cent). Our only case was a very large lesser curvature ulcer in an elderly physician with a bad heart, which was recognized at once as a dangerous ulcer on account of its size, but was considered inoperable by both patient and surgeon, and was not controlled by medical treatment. This case was not proved pathologically, but the clinical evidence of a cancer developing on a gastric ulcer seemed reasonably clear.

We began our medical treatment of gastric ulcer with private patients where the surgeon hesitates, such as young persons, old ladies, high lesser curvature cases and gradually extended it to some others, especially small lesser curvature ulcers.

Any physician who attempts medical treatment of gastric ulcer must do it with his eyes open and with a due sense of responsibility and a willingness to follow his cases with painstaking care by means of Roentgen ray examination, blood tests, tests of the empty-

ing of the stomach and so forth. If this is done, medical treatment is reasonable and safe, favorable cases are continued on medical treatment and unfavorable ones are promptly weeded out and referred to a surgeon. We have had no serious mistakes under this scheme, no serious complications, no unexpected cancer developing on our ulcers under continued medical treatment.

The life history of gastric ulcer under medical treatment is very interesting. We often see a rapid disappearance of the ulcer deformity in one or two months. This is readily shown by the Roentgen ray in lesser curvature ulcers, and has been verified by operation, where this has been occasionally done after a few weeks of medical treatment. In gross appearance we might even compare the active ulcer to a boil with much irritation and infection, with much round-cell infiltration and swelling. In a month or two we find the swelling all gone, the crater filled up, the ulcer flat and little but scar tissue left (Figs. 1 to 6).

Treatment of Hemorrhage and Obstruction. HEMORRHAGE. We all agree that medical treatment of the first gross hemorrhage in ulcer is much the safest and best. Nine cases out of 10 recover from acute hemorrhage, even if large. We all agree that patients who have recurrent hemorrhages under careful medical treatment need surgery, preferably excision. Transfusion of blood has made the operation in such cases far safer than in the past.

An occasional serious dilemma is probably unavoidable even with early surgical consultation. Operation may be delayed in the hope of getting the patient in better condition and another hemorrhage may cause death before or after the operation is done.

The details of medical treatment are the old-fashioned ones, absolute rest, opium, low liquids, low stimulation, rectal feeding for a day or two with the important addition of transfusion of blood. We do not use coagulants, such as rabbit serum, preparations of fibrin ferment or platelets, because these coagulants are not only abundant in the blood after acute hemorrhage, but usually increased in amount. Small doses of adrenalin by mouth are too much diluted before they reach the stomach to have much local effect.

PYLORIC OBSTRUCTION. This is due in one-tenth of the cases to organic tissue narrowing, in nine-tenths to spasm (W. J. Mayo). Such cases are especially important and deserve careful hospital management. We judge the case in regard to medical treatment by the amount of gastric residue at the start and by the response to treatment. Those with residues of 50 per cent or more, six hours after a barium meal, and those with considerable food residues, twelve hours after a motor meal, are usually surgical, and cases with twenty-four-hour barium residue are practically always surgical. Unless six-hour residues disappear in a few weeks, surgical treatment is usually best; we owe it to our patients to get them

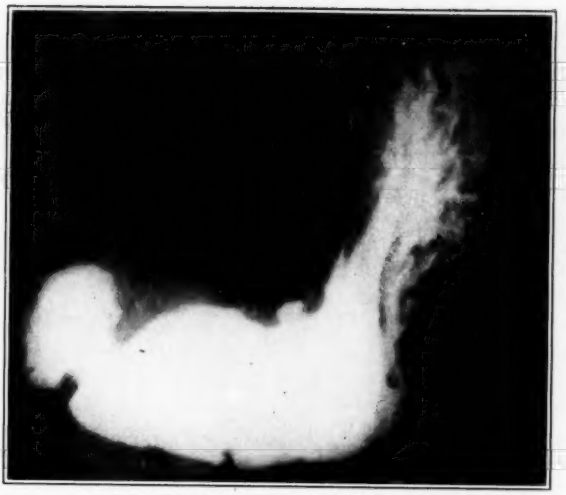

FIG. 1.—(Case I.) Medium-sized gastric ulcer on the lesser curvature at the beginning of medical treatment.

FIG. 2.—(Case I.) Five days later: Slight change; ulcer a little flatter, crater less deep.

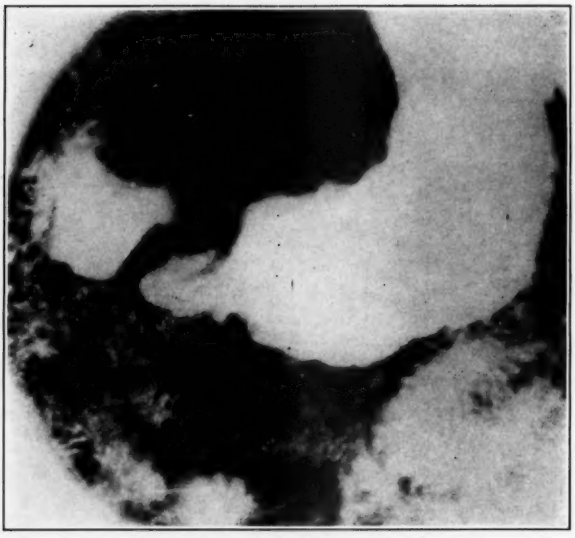

FIG. 3.—(Case I.) One month later: Marked change; ulcer deformity almost gone, a trace of the crater remains.

FIG. 4.—(Case I.) Six months later: Ulcer deformity entirely gone; patient well for five months (has continued well for three years).

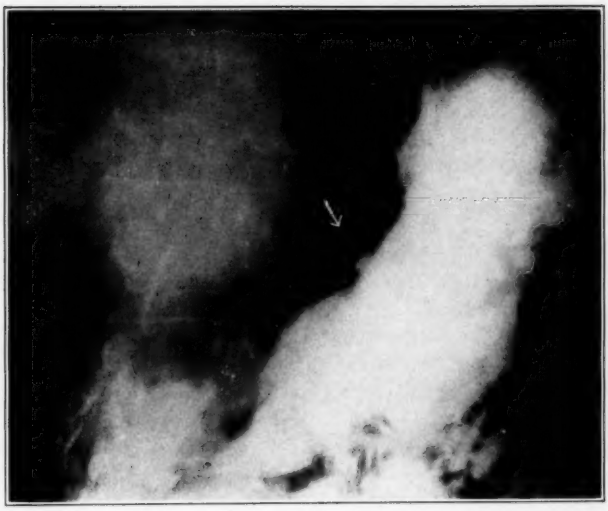

FIG. 5.—(Case II.) Medium-sized gastric ulcer on the lesser curvature at the beginning of medical treatment.

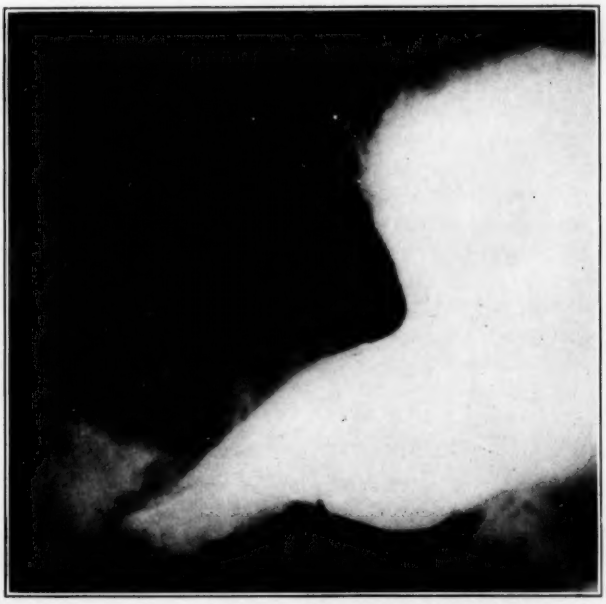

FIG. 6.—(Case II.) One week later: Ulcer deformity entirely gone. Patient is symptom free. (Seven other plates of the stomach taken at this time, at all angles, showed no deformity.)

well in the easiest and safest way, and not to carry medical treatment too far.

We do not use evening or night intubation to remove food residues or excessive acid secretion, as suggested by Sippy. If pyloric spasm does not relax on a bland diet, frequent feedings, rest in bed, alkalies and atropin without intubation, and the stomach does not empty itself normally in two to three weeks, then we usually advise gastroenterostomy, because the chances of recurrence under further medical treatment are large.

There are some patients, however, whose recovery from obstruction is slower, but still satisfactory. They have few symptoms, and may refuse operation and leave the hospital with 30 or 40 per cent six-hour residues after a barium meal. Such patients are always a source of anxiety, but quite often the spastic obstruction slowly, but completely, disappears within one or two months, and the patients remain entirely well for long periods.

There is a definite toxemia in some high-grade cases of pyloric obstruction, which is very serious and important, but fortunately rather rare. We have had little experience with it, having discovered only 2 cases in the last three years, in spite of careful chemical studies in all our cases of pyloric obstruction. This toxemia has been carefully studied by Berkman, Brown, Eusterman, Hartman and Rowntree and by McVicar, of the Mayo Clinic.

The clinical picture is characterized by vomiting, dehydration, shocklike features (prostration, low delirium, low blood pressure, red facies, high hemoglobin), uremia and often by tetany. There is a serious toxic nephritis with a lessened output of the urine, which contains albumin and casts, a low phenolsulphonephthalein excretion and important changes in the blood chemistry, such as high-blood urea nitrogen, low-blood chlorids and an invariable tendency toward alkalosis. Study of the blood chemistry is a more accurate way of measuring severity than the clinical appearance, and enables us to recognize the condition early and watch the progress of treatment.

In treatment, water is indicated to combat dehydration, to counteract shock, to promote diuresis and wash out nitrogenous waste products. Liberal doses of sodium chlorid are given, and sugar has been used to spare the protein. Sodium chlorid, 10 gm., glucose, 100 gm., and water, 1000 cc., are given intravenously or by rectum, once, twice or three times a day, and sodium chlorid solution is given subcutaneously and by mouth. Frequent lavage is used to clean and empty the stomach. Since all cases show a tendency to alkalosis, the use of alkalies is contraindicated. This has proved a very valuable preoperative medical treatment in cases of serious pyloric obstruction, and has greatly reduced the mortality at operation (from 16.5 to 0.6 per cent) at the Mayo Clinic in this limited group.

The presence of alkalosis and toxemia in these serious cases of pyloric obstruction is not, however, a logical argument against the reasonable use of alkalies in the average case of gastric ulcer.

One way to improve our results in ulcer is by earlier diagnosis. These long histories of five to ten years' duration are a reproach. We should give our patients earlier and better treatment; if medical will not do, then surgical. Better medical treatment does not mean a new diet or new drugs, but insistence on frequent feedings, better care in remissions, better education of the patient and a better follow-up system.

Many gastric ulcers are best treated surgically. In our whole series of 51 patients, 9 were operated upon at once and 10 more were operated upon later after medical treatment, making 37.2 per cent in all. We also feel sure that many gastric ulcers get a good lasting result with medical treatment without taking undue risk. In our series of 41 patients on medical treatment 40 per cent consider themselves well at the end of three to five years or more, and 29 per cent more are so much better that they have been unwilling to undergo operation.

It is not necessary to treat gastric ulcer with the idea that large numbers will become cancerous. We have only 1 case in the total series of 51 patients, including those operated upon at once and also those put upon medical treatment who have been followed for from three to five years or more.

A combined medical and surgical routine is the only logical one, medical for the large group of younger, milder uncomplicated cases; surgical for the chronic, serious resistant cases. The value of surgery is not in treating the whole group, but in curing so many difficult cases.

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CHRONIC DUODENAL ILEUS.*

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During the past six years considerable interest and not a little controversy have been aroused over the significance of the dilated duodenum and the question as to whether in the condition designated "chronic duodenal ileus" we have a true pathologic and clinical entity. We are all familiar with the importance of the duodenal segment of the gut, with the toxicity of its content when obstructed, and the grave and often fatal constitutional disturbances which follow a complete blockage of its lumen. In cases of so-called gastromesenteric ileus we have both clinical and postmortem evidence that an organic obstruction of the third part of the duodenum by the root of the mesentery is the active factor in producing the ileus. Thus the emptying of the stomach and the elevation of the pelvis in the prone or lateral position will immediately relieve the condition, and, in fatal cases, the postmortem examination will reveal the stomach and the duodenum, up to the mesenteric root, greatly distended while the bowel beyond is collapsed and empty.

That other forms of acute dilatation of the stomach and the upper reaches of the bowel occur is more than probable, and is no argument against the existence of the one with which we deal here. The rotation of the colon in fetal life, which brings the superior mesenteric vessels to lie athwart the duodenum, is subject to great variation. Imperfect rotation and fixation of the colon are found most frequently in subjects of the asthenic and visceroptotic type and, consequently, it is in this class of individual that duodenal ileus is most commonly met with. The small intestine, with its fluid content, is tolerant of handicaps to the onward passage of its chyme up to the point of complete obstruction, when it manifests its disability in no uncertain fashion. Thus we find a moderate duodenal obstruction persisting for years without symptoms sufficiently dramatic to incriminate the lesion until, finally, a complete obstruction supervenes with symptoms too obvious to be mistaken.

Pathologic Anatomy. Any abnormality of the mesentery will be liable to cause duodenal compression. Thus, the most marked case of duodenal ileus with which I have met was that of a boy aged seven years, in whom, owing to an abnormal rotation of the bowel, the duodenum was twisted sharply around the mesenteric vessels with resultant recurring attacks of complete duodenal obstruction which brought him frequently to the point of death.

* Read at Cleveland before the Inter-State Post-Graduate Assembly, October, 1926.

These attacks were finally stopped by short-circuiting the bowel around the difficulty. Any factor which allows of an undue drag on the mesentery may lead to duodenal compression. Congenital or acquired visceroptosis allowing of the small intestines sinking into the true pelvis without resting on the pelvic floor, a mobile proximal colon which sags into the pelvis and exercises traction on the mesentery, loss of supporting fat and defective bodily posture, all tend in greater or less degree to make the duodenal exit narrow and the passage of its content precarious. Chronic inflammatory fibrous thickening of the root of the mesentery, tuberculous adenitis and progressive or retrograde infiltration of the mesenteric pedicle by malignant disease, have all in my experience been the causative factors in producing a chronic duodenal ileus. Whatever the obstructive factor, dilatation of the first three parts of the duodenum is the striking feature. Hypertrophy of the wall may be encountered; it is, however, in my experience, not the rule. The pylorus is almost always widely patent and the stomach dilated. When the transverse colon is thrown upward the abdomen appears empty, the small intestines lying in the pelvis; the third part of the duodenum, however, bulges forward into the wound in unmistakable prominence.

Associated Lesions. Duodenal ileus would appear to predispose to ulceration in the stomach and duodenum. Out of 75 cases in which the dilated duodenum was exposed, in 12 cases one or more ulcers were present in the duodenum, in 4 cases a gastric ulcer was found, and in 3 cases both gastric and duodenal ulcers were present; that is, in 19 cases out of 75, or in 25 per cent of cases, there was coincident ulceration. In 4 cases, all in females, there was coincident cholecystitis with gall stones.

Sex and Age Incidence. Of the 75 cases with which I have met, 23 were in males, 52 in females. The average age at the time of operation was thirty-eight years in the males, forty-one years in the females; the youngest patient a boy, aged seven years, the oldest a man, aged sixty-six years.

Symptomatology. The clinical picture in this condition, while characteristic in the pronounced cases, is often ill-defined and difficult to differentiate. The one symptom to which I find constant reference made in the case records is epigastric fulness and flatulence coming on a short time after meals. As this symptom is also common to gall bladder disease, confusion must frequently arise. Pain is usually complained of, starting about half an hour after food, and felt usually just to the left but sometimes to the right of the umbilicus. Vomiting is not a constant symptom; when it does occur it is usually in periodic bouts, recurring every four or five weeks and lasting for from twenty-four to forty-eight hours at a time. Such attacks are described as severe bilious attacks. They are ushered in by malaise, headache and complete

loss of appetite. The vomiting is repeated and copious, bilious in character and leaves the patient weak and prostrated. Rapid improvement and a longer or shorter period of relief follows such an attack. Not infrequently these attacks date back to early childhood and are regarded as constitutional or as evidence of recurring acidosis. Such attacks may disappear during late adolescence and the patient may enjoy comfort for ten or fifteen years, when there appear the flatulent symptoms which bring the patient to seek relief. This late reappearance of symptoms may follow child-bearing, some illness, such as influenza, or periods of mental worry associated with deficient muscular exercise and fresh air, in fact with any condition which tends to lower the tone of the abdominal muscles and to favor visceroptosis.

Some patients discover that by adopting the recumbent position and raising the pelvis the discomfort and feeling of distention are relieved, a few state that they have found that kneeling and lowering the shoulders allows the flatulence to pass on. The persistence of the symptoms, the failure of dietetic measures to relieve them, the dread of eating induced by the inevitable discomfort which follows, all tend to make the patient nervous and frequently neurasthenic. The primary symptoms may come to be obscured by others of reflex or purely nervous origin, and the history in such cases is very difficult to assess and to disentangle. Further, the condition may be complicated by duodenal or gastric ulcer or both, or by biliary disease with a resultant symptom complex, hard to evaluate.

Physical Signs. The patient is usually spare and of slender build with narrow costal angle and broad pelvis. The stomach is found to be low, often dilated and splashing. Definite epigastric fulness may be visible at the time of examination. Splashing and gurgling in the duodenum may be elicited. It is exceptional to find, however, and I have been able to demonstrate it in only 4 cases. Definite tenderness is found in the majority of cases at some point, either just to one side of or above the umbilicus. Palpation of the lower part of the abdomen may determine the presence of a large dilated cecum in some cases.

Roentgen Ray Evidence. One might reasonably imagine that a hold up of the barium meal in the duodenum would be the inevitable and necessary evidence of a duodenal ileus. In the majority of cases it is so, and the dilated duodenum, outlined by its opaque content, is best seen about one and a half hours after ingestion of the meal. A fairly characteristic picture is to see, four hours after a barium meal, a saucer-like residue in the dilated first and third portions of the duodenum. In some cases, however, where recurrent attacks of sickness form the outstanding feature in the history, a Roentgen ray examination in one of the intervals of freedom may fail to show anything suggesting a real duodenal obstruction. Undoubtedly the most satisfactory results, following operative treat-

ment, have been in those cases in which there was obvious Roentgen ray evidence of duodenal stasis.

Differential Diagnosis. Duodenal ileus is most liable to be confused with gall-bladder trouble, and in many of my earlier cases the abdomen was opened with a diagnosis of cholecystitis. The use of cholecystography has narrowed the margin of error very considerably. In a number of cases a wrong diagnosis of duodenal or gastric ulcer had been made. The frequency of coincident ulcer and ileus, however, makes the differential diagnosis none the easier.

Operative Diagnosis. The problem of diagnosis is by no means always solved once the abdomen is opened. In the pronounced case, where the widely dilated pylorus and bulging first portion of the duodenum immediately present in the wound, and where on throwing up the transverse colon the abdomen appears empty but for the dilated third part of the duodenum which rises to the level of the abdominal wall, there is little difficulty in recognizing the trouble or determining the line of treatment. In not a few cases, however, where the symptoms and signs have been merely suggestive and where a visceroptosis, with a moderate dilatation of the duodenum, is the only abnormality discoverable, the surgeon is in two minds as to the diagnosis and as to the propriety of performing a duodenojejunostomy. It is in such cases that the demonstration of a definite obstruction by the root of the mesentery is so difficult and uncertain. The methods of inflating the stomach and duodenum by passing air through a stomach tube with the parts exposed to view, which I practised at one time, I have now discarded as the evidence which it gives is, I believe, untrustworthy. In 21 such doubtful cases I have performed the operation of duodenojejunostomy. The result has been very good in 5; in 8 cases the patients have been much improved and in the remaining 8 cases the patients still complain of their old symptoms.

Treatment. So many factors and pathologic conditions may result in duodenal stasis that no one line of treatment is suitable for all. In the common type, where visceroptosis is the primary cause, conservative and postural treatment will relieve or cure a considerable number of patients. The importance of postural treatment on the lines so ably worked out and practised by Goldthwaite, alone or combined with operative treatment, cannot be too strongly emphasized. I have had the benefit of the assistance of Mr. W. A. Cochrane, a pupil of Goldthwaite, in the management of some of my cases, and I have been greatly impressed with the results of his postural methods. Many cases, however, are seen too late to be cured by physical measures, short of operation, and in these the performance of a duodenojejunal anastomosis is, I believe, the operation of choice. Where a mobile proximal colon has sagged into the pelvis a colopexy may give relief but is not as

certain as where a duodenal anastomosis is carried out. Where the duodenal obstruction is due to an infiltration of the mesenteric root by simple inflammatory, tuberculous or malignant disease a duodenojejunostomy is the only rational operation.

Duodenojejunostomy. This operation, first suggested by Barker and Bloodgood and first performed by Stavely, I have carried out in 64 cases of duodenal stasis. The operation is easy to perform in the suitable case; difficulty of access usually means a questionable indication. The anastomosis may be made either submesocolic antiperistaltic or transmesocolic isoperistaltic. In the majority of cases the former is the more suitable; in some, however, the dilated second part of the duodenum, reached through the transverse mesocolon, presents itself more readily for anastomosis. In my series there were 57 submesocolic antiperistaltic and 7 transmesocolic isoperistaltic operations. No appreciable difference in the after results could be found in the two series. Whichever operation is performed a free mobilization of the duodenum is desirable. Angled clamps may be employed but lately I have discarded the use of clamps in many cases. In all but the first few cases, No. 00 twenty-day catgut or the eyeless needle has been used for both layers of sutures.

In a number of cases the duodenojejunostomy was associated with other procedures. In 5 cases with duodenal ulcer a gastroenterostomy was also performed, in 1 case a gastroduodenostomy. In 1 case where old gastric and duodenal ulcers had caused hourglass contractures of stomach and duodenum a gastrogastrostomy and a gastroduodenostomy were performed as well. In 4 cases a coincident cholecystectomy was performed and in 1 case a cholecystectomy and choledochotomy. These multiple procedures were well tolerated and did not contribute to the mortality.

Postoperative Treatment. In the asthenic and visceroptotic type of patient, so prominent in the duodenal ileus group, the operation of duodenojejunostomy, when necessary, should form only an incident in the course of treatment. After the immediate convalescence from operation the patient should wear a suitable abdominal belt and should undergo a course of postural treatment, which will effect an immense benefit, both to the abdominal condition and to the general tone and morale. I confess that in many of my cases too little care was given to the after-treatment and in such cases, after a temporary improvement, a recurrence of symptoms was reported.

The immediate result of the operation is, as a rule, eminently satisfactory. Little postoperative trouble is encountered and the mortality is low. In this series of 64 cases there were 3 hospital deaths. In 1 case a very feeble patient, who had suffered from persistent vomiting after a gastroenterostomy performed two years previously, the patient died two weeks after the operation from

peritonitis, following a rupture of the abdominal wound with prolapse of the intestines. In a second case the patient died from shock following an extensive resection of the small intestine for tuberculosis; a duodenojejunostomy was performed as well, as the duodenum was greatly dilated from pressure by glands at the root of the mesentery. In the third case the patient suffered from exophthalmic goiter. Persistent bilious vomiting for three months was attributed to pressure on the duodenum by calcareous tuberculous glands in the root of the mesentery shown by Roentgen ray. The patient recovered from the abdominal operation but died after a subsequent operation on the thyroid while still in hospital. The dilatation of the duodenum in this case was not very great and the abdominal operation was ill advised and undoubtedly had a malign influence on the thyrotoxicosis. It must, therefore, be included in the mortality list. A fourth death might also with some reason be included, that of a patient who died of pneumonia two weeks after leaving hospital. In spite of these deaths, all of which occurred in cases complicated by other trouble, the operation may be ranked as one of the safest in abdominal surgery. The convalescence is, as a rule, smooth and uneventful, more so than in the case of gastroenterostomy.

Ultimate Results of Duodenojejunostomy. The cases dealt with in this paper were all operated upon between February, 1921, and July, 1926. In more than half of them periods of from three to five and a half years have elapsed since operation. A recent *questionnaire* as to their present state has given the following facts:

Excluding 7 cases, 3 of which were not traced and 4, which, although well, are too recent for comparison, there remain 57 cases. Of these 23 patients reported that they were cured of their former trouble, had gained in weight—1 as much as 49 pounds—had no vomiting or digestive trouble. In 11 cases the patients reported themselves as very much improved, although having occasional flatulence and pains. In 12 cases the report was of improvement tempered with occasional digestive trouble. In 9 cases there was either little improvement or relapse after a temporary benefit. In this latter group of unsatisfactory cases were included the marked visceroptotics, some of whom had had several previous operations, and in whom the operation of duodenojejunostomy was performed in the hope that it might benefit, although the indications for it were somewhat indefinite.

The best results were undoubtedly in those cases where, prior to operation, there was definite roentgenologic evidence of duodenal stasis. Where associated with gastroenterostomy for duodenal ulcer with ileus, the results were uniformly good. In 3 cases in which secondary duodenal ileus was caused by malignant infiltration of the root of the mesentery, the primary growth being in the lesser curvature of the stomach, great relief was given for periods of

from four and a half months to seven and a half months, when death resulted from widespread disease.

Conclusions. In reviewing this group of cases one finds that where the duodenum was found at operation to be obviously obstructed by some more or less gross anatomic abnormality or pathologic process in the root of the mesentery, the results of a short-circuiting operation were excellent. Where the duodenum was found dilated, but no very obvious obstructing cause was visible, the short-circuiting operation gave most uncertain results. In many, an early improvement was followed by recurrence of symptoms. In no case, however, was the patient made worse by the operation.

A dilatation of the duodenum may apparently be present without any detectable mechanical obstruction, for reasons as yet unknown, and the drainage operation in this class of case is relatively ineffective. In the visceroptotic individual with signs of duodenal ileus, postoperative physical and especially postural treatment is essential for complete and lasting relief.

ACUTE INTESTINAL OBSTRUCTION: MECHANISM AND SIGNIFICANCE OF HYPOCHLOREMIA AND OTHER BLOOD CHEMICAL CHANGES.

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No surgical problem has caused more controversy than intestinal obstruction. None has been more thoroughly studied. Yet, if any one fairly familiar with the recent literature on this subject will read Kocher's[1] paper published in 1898, he will be astonished by how little our knowledge has increased in the last thirty years. There is still no agreement among authorities as to the cause of death in acute intestinal obstruction.

The problem has proved to be extremely complex. For many years it was attacked as a whole, as if there were but one type of obstruction and one cause of death. This narrow viewpoint has hindered progress. Recent writers have begun to modify it. Of late much attention has been devoted to the changes in blood chemistry found in acute intestinal obstruction. This paper is a report of an investigation covering this phase of the subject.

Historical Review. McCallum and coworkers[2] in a series of experiments, begun as early as 1909, called attention to the relationship between gastric tetany and pyloric obstruction. They found the mechanism to be an increased alkalinity of the blood, and a marked reduction of the plasma chlorids due to the loss of hydrochloric acid through vomiting. More recently Haden and Orr[3] have made a valuable contribution to our knowledge by pointing out that these same changes occur in acute obstruction of the small intestine. They have shown that there occurs a marked fall in blood chlorids and a subsequent increase in the urea and total nonprotein nitrogen, this increase being greatest in the last twenty-four hours of the animal's life. Accompanying the fall in chlorids there is a marked increase in the carbon dioxid combining power of the plasma (alkalosis). These changes are more pronounced in duodenal or high intestinal obstruction.

Our own observations have shown that these results can be duplicated repeatedly by following the technique outlined by Haden and Orr. In their interpretation, however, Haden and Orr[4] have chosen to assume that the fall in blood chlorids is due not to a loss or output of chlorids, but to a fixation in the tissues of the chlorin ion with a toxin from the obstructed bowel. This utilization of the chlorin ion they regard as a protective mechanism on the part of the body. The terminal increase in the nitrogenous elements of the blood, coming as it does after the chlorids are reduced, is, according to their views, an evidence that this protective mechanism has been exhausted.

They[4] support their views by reporting dogs with obstruction of the duodenum kept alive for twenty to thirty days by frequent hypodermic injections of solutions of sodium chlorid, whereas untreated controls died in from three to seven days. In their treated animals the other chemical elements of the blood remained normal as long as the chlorid level was maintained in this way.

Foster and Hausler[5] strongly attack the views of Haden and Orr. They maintain that the marked changes observed in the control animals of Haden and Orr occurred in the first five days, before the tissues damaged by the operation had time to heal. Foster and Hausler have reported two dogs with obstruction at the duodenum produced by cutting and inversion of the bowel under local anesthesia. These animals were then given physiologic salt solution hypodermatically during the first five days to tide them over this critical period of repair. Complete food, water and salt starvation was then begun. The animals lived a total of twenty-one and twenty-eight days respectively.

From this, Foster and Hausler concluded that death in uncomplicated cases of acute intestinal obstruction is due to dehydration and starvation, that there is no evidence of toxemia, and that hypochloremia is not present. Their statement concerning the blood chemistry we cannot substantiate.

We wish, however, to emphasize a view held by Foster and Hausler that there must be recognized two types of acute intestinal obstruction: (1) Acute simple obstruction in which there is complete blocking of the lumen with no circulatory involvement; (2) acute strangulation in which there is interference with venous, arterial and lympathic circulation as well as obstruction to the intestinal lumen. The morbid processes involved and the symptoms thereof are widely different in these conditions. For these reasons, if for no other, the complex problem under the general term intestinal obstruction is merely made more confusing by any writing which does not differentiate these mechanisms. Obviously in most of the conditions which are designated as acute intestinal obstruction the actual mechanism is acute strangulation. Gall stones, enteroliths or other foreign bodies may completely occlude the lumen of the small intestine without the factor of strangulation but these form a relatively small precentage of cases. In all the commoner forms of obstruction such as volvulus, intussusception, hernia, twists or kinks, and adhesion bands, it is the strangulation and the ensuing gangrene which contribute most of the factors leading to death. In a later publication we shall hope to evaluate and coördinate these lethal factors. The present writing will be confined to the changes in the blood chemistry which occur in each form of acute intestinal obstruction.

Procedure. Dogs were employed in all experiments. The operations were performed with aseptic technique under morphin and ether anesthesia. Hausler[6] and Foster have criticized the use of these drugs, claiming that the first five days after operation constitute a critical period during which time the control animals die because they have to combat, not only the obstruction but also the anesthetic and the tissue damage of the operation. While there is some merit in this contention we feel that they have overemphasized it. Dogs withstand ether anesthesia and abdominal surgery remarkably well. Great numbers of dogs recovering from intestinal anastomosis may be taken as controls of this fact.

One animal we purposely subjected to a long anesthetic, during which time the duodenum was divided and a lateral anastomosis done, an awkward operation causing much trauma and tending to produce a bad functional result. This animal (Dog 41) recovered promptly, never vomited at any time and showed no changes in blood chemistry.* Since this dog served as a general control we give the blood chemistry in Table I.

* The chemical analysis of our experiments were conducted by W. S. Fisher in the Department of Biochemistry, Indiana University School of Medicine, under the supervision of Dr. B. B. Turner and Dr. R. N. Harger. Urea nitrogen in the blood was determined by method of D. D. van Slyke and G. E. Cullen (J. Biol. Chem., 1914, **19**, 211). Total nonprotein nitrogen by method of Folin and Wu (J. Biol. Chem., 1919, **38**, 81). Sodium chlorid in the blood by method of Whitehorn (J. Biol. Chem., 1921, **45**, 449). Sodium chlorid in the urine and vomitus output by a slight modification of the same method. Total nitrogen in the urine by method of Folin and Denis (J. Biol. Chem., 1916, **26**, 473).

TABLE I.

(Dog 41. Division of the duodenum with lateral anastomosis.)

Remarks.	Day.	Mg. per 100 cc. blood.			Urine output.	
		Urea nitrogen.	Total nonprotein nitrogen.	NaCl.	Quantity, cc.	NaCl, gm.
Day of operation	0	9.6	29.8	568		
No food or water	1	14.5	34.9	534	320	3.12
No food or water	2	15.0	40.2	536	300	2.17
Water *ad lib.* and milk	3	14.1	40.0	547	170	0.27
Water *ad lib.* and milk	5	10.2	30.3	503	1100	0.76
Water *ad lib.* and milk	7	16.1	40.0	546	1070	3.30
Animal at large	56	15.6	36.6	490		

It will be noted that this animal continued to excrete sodium chlorid in the urine normally for two days despite the fact that no food, water, or salt was given during this period. There was only a slight reduction of blood chlorids. This may be due, no doubt, to the fact that there was an abundance of salt in his gastro-intestinal tract at the time of operation. Also, due to dehydration, the actual decrease would be concealed by a moderate concentration in his blood. On the third day the excretion of chlorids fell practically to *nil*. With the administration of water there was a marked increase in urine but yet practically no excretion of chlorids. The blood chlorids, however, showed a more pronounced fall due to the proper dilution of the blood. Then with the administration of milk, the blood and urine chlorids regained their former level. The animal was at large in the pens two months, at the end of this time there were no abnormal or significant changes in blood chemistry.

In all, 54 dogs were used. After testing various methods of producing obstruction, the plan of dividing the bowel and inverting the ends was finally adopted to produce an acute simple obstruction. In the study of obstruction plus strangulation various methods were employed as will be described later.

The Reduction of Blood Chlorids and the Increase in Nonprotein Nitrogen. At the outset let us state that we soon discovered the changes in blood chemistry to be largely dependent upon the postoperative course of the animal. Our findings varied chiefly according to whether or not the dog was given water. We can, perhaps, present our observations most clearly in the form of a series of propositions to each of which is appended the supporting experimental evidence.

1. *There is usually no appreciable decrease in blood chlorids until after forty-eight hours. Thereafter the reduction is greater the*

longer the animal lives without the administration of salt. The reduction of blood chlorids is directly proportional to the chlorids lost by the animal, which occurs chiefly through vomiting. The loss through vomiting is greatest in dogs allowed water by mouth ad lib.

The following protocols give data which is typical of our findings under the conditions described. No effort was made to control the food or water intake of these animals before operation. The preöperative dose of morphin however always produced vomiting which emptied the stomach of any grossly undigested food. The animals were kept in metabolism cages in which the total output of urine and vomitus could be collected.

Dog 37.—Obstruction of the duodenum; no water, food or salt given. The animal showed no signs of tetany, but died at the end of sixty-five hours in a state which seemed due chiefly to dehydration. Autopsy showed a superficial wound infection and distention of the duodenal stump, in which there was some discoloration. The chemical findings are given.

Dog. 38.—Obstruction 12 inches above the cecum. No food, water or salt given. In this animal also there were no demonstrable symptoms of tetany. He died at the end of sixty-nine hours in much the same condition as Dog 37, a "toxic" state with frequent vomiting of brownish fluid in small quantities, the heart rapid and bounding and extremities pulseless. Autopsy showed acute simple obstruction, but with some distention and discoloration of the proximal stump. There was no actual gangrene and no peritonitis. The findings are given in the table.

TABLE II.

(Intestinal obstruction; water withheld.)

Remarks.	Day.	Mg. per 100 cc. blood.			Vomitus.		Urine.	
		Urea nitrogen.	Total nonprotein nitrogen.	NaCl.	Quantity, cc.	NaCl, gm.	Quantity, cc.	NaCl, gm.
Dog 37 (obstruction at duodenum; water withheld)	0 . . .	10.7	37.7	515				
	1 . . .	4.9	36.5	482	1010	6.76		
	2 . . .	36.4	65.5	432	320	2.40		
	3 . . .	87.2	142.8	440	200	1.50		
						2.60*		
	Total .	...	...	...	...	13.26		
Dog 38 (obstruction of ileum; water withheld)	0 . . .	8.3	28.2	523				
	1 . . .	6.1	33.3	450	770	4.10	130	0.52
	2 . . .	23.5	66.2	392	610	5.04		
	3 . . .	50.9	117.6	384	490	4.16		
						2.30*		
	Total .	...	...	...	...	15.60	...	0.52

* Washings from pen.

Dog 36.—Obstruction at the duodenum in the same manner as Dog 37. Water allowed by mouth *ad lib.* There was no other treatment. The symptoms displayed by this animal were much different from those seen in animals which had no water. This dog drank much water and vomited it freely. For the first sixty to sixty-four hours postoperative his condition remained good. Then he began showing signs of tetany, first a rigor of the jaw in attempting to drink, and a stiffness of the legs. At seventy hours tetany was marked, there were constant twitchings and spasms of all the muscles, breathing was slow and dehydration was marked. At seventy-nine hours the animal was rigid and prostrated, respirations were very rapid and shallow, becoming slow and superficial toward the end. Rigor mortis was present when the dog died at the end of eighty hours. Autopsy showed acute simple obstruction of the duodenum, with no evidences of peritonitis; all parts of the bowel normal in color, the upper segment only slightly distended. (See Table III.)

Dog 42.—Obstruction 12 inches above the cecum. Given water by mouth *ad lib.* The postoperative course and symptoms were similar to those of Dog 36. This animal lived about ninety-two hours. The autopsy showed simple complete obstruction of the ileum, with no complications. (See Table III.)

TABLE III.

(Intestinal obstruction; water *ad lib.*)

Remarks.	Day.	Mg. per 100 cc. blood.			Vomitus.		Urine.	
		Urea nitrogen.	Total nonprotein nitrogen.	NaCl.	Quantity, cc.	NaCl, gm.	Quantity, cc.	NaCl, gm.
Dog 36 (obstruction of the duodenum; water by mouth, *ad lib.*)	0	14.70	40.5	482				
	1	6.10	32.9	450	350	3.25	150	0.75
	2	13.80	58.2	351	2950	12.68	60	Trace
	3	38.50	130.0	246	1360	5.79		
	4	88.60	165.6	205				
						2.11*		
	Total	...	...	...	...	23.83	...	0.75
Dog 42 (obstruction of ileum; water by mouth *ad lib.*)	0	13.25	40.2	490				
	1	9.20	41.6	419	1250	4.20		
	2	7.50	29.3	434	1550	4.65		
	3	11.84	45.1	389	730	3.00		
	4	62.90	95.2	278	800	2.05		
						3.40*		
	Total	...	...	...	...	17.30		

* Washings from pens.

From these experiments it will be noted that a large excretion of chlorids ensues promptly with the vomiting. With some effort the urine and vomitus were collected in separate ends of the cages in a sufficient number of cases to assure us that in these obstructed animals the quantity of urine excreted is small, and the chlorids

lost in that way are negligible. The vomiting, however, has always produced a definite loss of chlorids, greatest in those animals allowed water *ad lib.* These dogs will literally wash out their chlorids by drinking and vomiting large quantities of water and their reduction of blood chlorids is correspondingly greater. Dog 37, (Table II), showed a loss of 13.26 gm. of sodium chlorid, and at death his blood contained 440 mg. of sodium chlorid per 100 cc. Whereas, Dog 36 (Table III), allowed water *ad lib.* by mouth, lost 23.83 gm. and reduced his blood chlorids to 205 mg. per 100 cc. In all of these animals dehydration was marked.

These animals have all shown a greater output of chlorids than has been reported by Haden and Orr. We believe that this may be due entirely to the chlorid intake just previous to operation. They report that in their animals food was withheld for forty-eight hours previous to operation, whereas, in this series there was no preoperative starvation. This would undoubtedly alter the chlorid content of the bowel at operation, and we feel that it accounts for the discrepancy in our findings. Dog 41 (Table I), in which there was no obstruction and no preöperative starvation, excreted in the urine more than 5 gm. of sodium chlorid in forty-eight hours without appreciable change in the chlorid content of the blood. The excretion then fell off sharply, being resumed again when food was taken. As opposed to this, Dog 28 (Table IV), which was starved for twenty-four hours, obstructed at the duodenum, and allowed water by mouth *ad lib.*, died after seventy-two hours, having reduced the chlorids to 351 mg. with an output of only 6.67 gm. Obviously the amount of excess sodium chlorid possessed by the animal will modify the blood changes resulting from any loss which he may undergo.

TABLE IV.

(Dog. 28. Starvation for twenty-four hours preöperative; obstruction of the duodenum; water by mouth, *ad lib.*)

Day.	Mg. per 100 cc. blood.			Vomitus and urine.	
	Urea nitrogen.	Total nonprotein nitrogen.	NaCl.	Quantity, cc.	NaCl, gm.
0	8.6	35.5	489		
1	7.7	52.5	442	330	1.87
2	37.2	107.1	368	1251	2.50
3	77.4	203.4	351		2.30*
Total	...	...	...	...	6.67

* Washings from pen.

It appears that in the starving animal the chlorids quickly reach a level of equilibrium with little or no reserve. In such a case a relatively small loss causes a reduction of blood chlorids. This loss is quickly accomplished by vomiting, in the obstructed animal where the hydrochloric acid secreted by the stomach has no chance for reabsorption. A potential loss may even be accomplished without vomiting if this chlorid laden secretion is retained in the obstructed stomach and upper bowel. We have repeatedly analyzed the contents of the obstructed bowel for sodium chlorid, finding 700 to 900 mg. per 100 cc. In this connection it is interesting to note that obstruction at the sigmoid causes neither vomiting nor reduction of blood chlorids.

Dog 34.—Obstructed at the sigmoid by cutting and inversion of the bowel. Water was allowed by mouth *ad lib.* There was no other treatment. There was no vomiting, and the animal's condition remained good for six days. Toxic symptoms then set in with fever, prostration and circulatory collapse. At autopsy on the seventh day all the intestinal loops were markedly distended, and there were patches of discoloration along the antimesenteric border. There was no peritonitis.

TABLE V.

(Dog. 34. Obstruction at the sigmoid; water, *ad lib.*)

Day.	Mg. per 100 cc. blood.			Urine.	
	Urea nitrogen.	Total nonprotein nitrogen.	NaCl.	Quantity, cc.	NaCl, gm.
0	6.4	22.0	495		
1	9.4	45.5	388	530	2.45
2	6.8	43.1	445	180	0.33
4	8.1	27.8	462	260	0.26
6	6.4	37.0	465	325	0.24
7	9.6	44.0	460		0.50*
Total	...	...	...	...	3.78

* Washings from pen.

In an obstruction of this type, the intestinal contents pass beyond the cecum where the absorption of the sodium chlorid together with the water may take place. As shown in Table V, there is, under these conditions, no loss of chlorids by vomiting and no hypochloremia, even though the obstruction be fatal.

In high intestinal obstruction there is usually a slight hypochloremia apparent at the end of the first day, but the reduction is not appreciable until after forty-eight hours. We have never observed tetany in these animals until after the sodium chlorid in the blood has fallen to a level of 350 mg. per 100 cc. Though we regard such a reduction of chlorids as a lethal factor, we do not feel that it bears any relationship to the "toxemia" of intestinal obstruction.

Certainly there is no evidence that the chlorids are fixed in the tissues by a toxin. In several dogs we have analyzed the liver and muscle tissue for chlorids[7] always finding a reduction comparable to the hypochloremia. It is probable that similar changes would be found in other tissues.

TABLE VI.

(Chlorids in the tissues.)

	Grams of NaCl per kg.	
	Liver.	Muscle.
Normal Dog A	3.23	0.95
Normal Dog B	3.22	1.05
Dog 37 at death	2.45	0.79
Dog 36 at death	1.00	0.36

In none of our experiments have we encountered evidence to indicate that the hypochloremia of acute intestinal obstruction results from any cause other than a loss of chlorids. This loss is accomplished by the retention of chlorids in the upper intestinal segment and by vomiting. The amount of chlorid loss necessary to cause hypochloremia depends upon the chlorid reserve which the animal has at the time of obstruction.

2. *A reduction of blood chlorids as marked as that which occurs in acute intestinal obstruction can be produced by the ligation of both ureters or the removal of both kidneys.*

Our data on nephrectomized dogs is given in Table VII.

TABLE VII.

(Blood chemistry in nephrectomy and intestinal obstruction; effect of sodium chlorid.)

Remarks.	Day.	Mg. per 100 cc. blood.		
		Urea nitrogen.	Total nonprotein nitrogen.	NaCl.
Dog 19 (bilateral nephrectomy; obstruction of the bowel 12 inches above cecum; profuse vomiting and convulsions on last day)	0	2.9	16.2	449
	1	61.9	100.0	439
	2	180.0	222.0	266
Dog 22 (ligation and division of both ureters; water by mouth, *ad lib.*; profuse vomiting; death in four days)	0	9.6	28.0	530
	1	54.5	67.0	509
	2	120.0	162.0	468
	3	169.7	214.0	425
	4	192.7	277.0	359
Dog 23 (bilateral nephrectomy; water by mouth, *ad lib.*; profuse vomiting and convulsions on last day)	0	18.8	32.0	469
	1	64.9	79.9	491
	2	106.2	171.0	400
	3	156.5	198.0	298
Dog 24 (bilateral nephrectomy; water by mouth, *ad lib.*; daily hypodermoclysis of 2 per cent NaCl solution; profuse vomiting; no convulsions observed)	0	14.1	34.8	521
	1	55.5	65.0	552
	2	71.0	139.0	500
	3	151.3	170.0	442
	4	178.0	270.0	531

In all of these animals there was frequent vomiting and a great reduction of blood chlorids. Dog 19, in which there was intestinal obstruction as well as double nephrectomy, showed a more rapid course, but the changes in blood chemistry were identical with those seen in the animals with nephrectomy only. The administration of 2 per cent salt solution to Dog 24 maintained for him a normal level of blood chlorids but had no effect on the increase of nitrogenous elements. Though unfortunately the chlorid output was not measured in these animals, we feel that here again the hypochloremia must be due to the loss through vomiting.

3. *Dogs with acute simple obstruction may be kept alive throughout the period of starvation by the hypodermic administration of sodium chlorid and water, but this treatment is of little or no value in cases of acute strangulation. The administration of salt to an animal with acute obstruction is of no avail if water is withheld.*

Haden and Orr have repeatedly demonstrated the value of solutions of sodium chlorid in acute intestinal obstruction, but we feel that the mechanism and limitations of this therapeutic effect need as adequate explanation.

Dog 44.—Obstruction at mid-duodenum. No food or water allowed. Ten grams of NaCl in 30 cc. of water injected hypodermically eighteen hours postoperative. Injection painful. Twenty-four hours later the same injection was repeated intravenously. Autopsy showed simple uncomplicated obstruction of the duodenum.

Dog 45.—Obstruction at the mid-duodenum. No food or water allowed. At the end of eighteen hours 10 gm. of NaCl was given intravenously in 30 cc. of water. On each succeeding day one-half that amount was given. Blood samples were drawn before and five minutes after the injection the first two days; on the third day the second blood sample was drawn at death, eight hours after the last injection of salt. Autopsy showed simple uncomplicated obstruction of the duodenum.

Dogs 35 and 40.—In these dogs a 12-inch loop of lower ileum was isolated by cutting and anastomosis of the bowel around it. The ends of the loop were inverted, the mesentery of loop was ligated and cut allowing the segment of lie free in the abdominal cavity. Dog 35, which received no treatment, died in sixteen hours. At autopsy the loop was in a state of anemic gangrene, foul smelling and of a pale brown color. The structures of the omentum and bowel, against which it had been lying, were gangrenous. All of the abdominal structures were inflamed, but there was no pus. Dog 40, which received a total of 2000 cc. of normal salt, lived twenty-five hours. Autopsy showed the loop almost entirely destroyed by the gangrenous process. There was generalized peritonitis.

In explaining the therapeutic effect of sodium chlorid Haden and Orr have assumed a specific neutralization of the toxins. They have shown that no other inorganic salt possesses this power to save the animal, and have also shown the administration of fluids without sodium chlorid is of no avail.

TABLE VIII.

(Obstruction of ileum 12 inches above the cecum; water by mouth, *ad lib.*; treatment as indicated in remarks.)

Remarks.	Day.	Mg. per 100 cc. blood.		
		Urea nitrogen.	Total nonprotein nitrogen.	NaCl.
Dog 18 (allowed water by mouth, *ad lib.*, but no salt; tetany developed rapidly; autopsy on third day showed acute simple obstruction of the ileum)	0	12.3	22.4	579
	1	11.6	27.9	416
	2	13.0	23.1	257
	3 8 A.M.	22.8	75.9	228
	2 P.M.	61.5	103.7	211
Dog 17 (given daily by hypodermoclysis a total of 1000 to 2000 cc. of 1.8 per cent NaCl solution; dog in good condition; no toxic symptoms; on nineteenth day, under local anesthesia, an attempt was made to relieve the obstruction by enterostomy; the whole small intestine was thickened, but there was no strangulation or marked distention; death on twenty-first day from generalized peritonitis, as a result of the enterostomy)	0	9.2	20.6	560
	1	6.1	23.8	495
	2	6.2	20.1	486
	3	5.9	26.7	521
	4	5.5	16.6	521
	5	4.2	21.9	471
	6	4.4	16.9	512
	7	5.3	25.0	516
	8	4.1	19.1	535
	10	5.4	20.3	477
	12	6.3	20.1	481
	18	5.8	20.8	454
	21	7.4	23.3	830
Dog 26 (given water, *ad lib.*, by mouth, and 1000 to 1500 cc. of 2 per cent NaCl solution daily; autopsy on second day showed gangrene and perforation of the lower 2 inches of the obstructed bowel)	0	6.6	21.2	537
	1	4.2	24.1	504
	2	5.2	32.6	628
Dog 32 (1000 cc. of 2 per cent NaCl solution daily; condition good for six days; autopsy on seventh day showed great distention and discoloration of the lower 12 inches of the obstructed bowel; no actual gangrene)	0	13.7	48.0	466
	2	11.5	34.3	537
	4	10.7	34.5	478
	7	20.9	122.0?	468

All of their findings we have been able to substantiate, but we do not feel warranted in assuming any detoxifying action. Copher and Brooks[8] have shown that the contents of obstructed bowel are very toxic, causing death when injected intravenously. Also that animals receiving the injection show no changes in blood chlorids, and cannot be saved by the administration of salt solution. We have found it easy to prolong life in the animals with duodenal obstruction by the administration of sodium chlorid and water. In obstruction of the ileum, however, we have been able to accomplish this only once in our series. Dog 17 (Table VIII) responded to this treatment, whereas Dogs 26, 32 and several others were lost by the same treatment. Always where the treatment failed there

was found to be some damage to the bowel wall by overdistention or strangulation. This complication occurs much less readily in obstruction of the duodenum.

TABLE IX.

(Obstruction at midduodenum; water withheld; daily injection of saturated salt solution, as given in protocols.)

Remarks.	Day.	Mg. per 100 cc. blood.		
		Urea.	Total nonprotein nitrogen.	NaCl.
Dog 44:	0	13.6	36.8	513
Before injection	1	10.2	37.9	412
Before injection	2	63.0	91.4	468
After injection	3	60.9	98.8	637
Dog 45:	0	12.0	41.4	469
Before injection	1	10.3	35.5	400
After injection	1	9.5	34.7	579
Before injection	2	17.6	39.7	524
After injection	2	17.6	42.2	613
Before injection	3	31.8	54.6	614
After injection	3	45.0	80.0	724

TABLE X.

(Complete strangulation of 12 inches of ileum; treatment as indicated in remarks.)

Remarks.	Day.	Mg. per 100 cc. blood.			Vomitus and urine.	
		Urea nitrogen.	Total nonprotein nitrogen.	NaCl.	Quantity, cc.	NaCl, gm.
Dog 35 (no treatment; profuse vomiting)	0	7.5	34.2	502		
	1	6.4	44.4	335	650	6.44
Dog 40 (1000 cc. 0.9 per cent NaCl)	0	5.3	39.2	523		
	1 2 P.M.	7.2	36.4	542		
	1 11 P.M.	21.0	75.0	523		

We feel that in acute simple obstruction the intact mucosa of the intestine prevents absorption of the toxins from the lumen, hence there is no toxemia.[9] There is, however, rapid dehydration, loss of chlorids through vomiting and starvation. These in the order named are the lethal factors in acute simple obstruction. The giving of sodium chlorid solution by hypodermoclysis prevents death from dehydration and hypochloremia. However, with the slightest degree of strangulation the absorption of toxins ensues,

and the treatment with salt does not prevent death from this toxemia (Table VIII).

It is not our intention to underestimate the importance of sodium chlorid in the animal body under these or any other conditions. It is quite apparent that a proper concentration of this salt in the blood and tissues is indispensable in maintaining the normal osmotic relations and the entire fluid metabolism of the body. In those animals with a marked reduction of the chlorids, the blood becomes thick and dark, and we have found no means other than the administration of sodium chlorid *and water* by which this severe dehydration and other symptoms of hypochloremia can be prevented or relieved.

It is apparent also that the course of a toxemia, such as occurs in acute strangulation of the bowel, may be mitigated by transfusions of sodium chlorid solution as will be seen by a study of Table X. This action must be due to the support of the general circulation and to an increased elimination through the kidneys. The fact that the administration of sodium chlorid is of no avail if water is withheld would seem to disprove a specific detoxifying action (Table IX).

As additional proof of our interpretations the following experiment is cited.

Dog. 30.—The bowel was cut at the mid-duodenum and 12 inches above the cecum. The duodenum was then anastomosed to the ileum and the ends of the loop thus isolated were inverted, converting practically the entire small intestine into an obstructed loop with the lumen of the bowel reëstablished around it. The animal was allowed water, *ad lib.*, by mouth. For five days there was no other treatment. The dog vomited profusely, and on the fifth day was in tetany and very near death. Treatment, by hypodermoclysis, with sodium chlorid, was instituted as indicated in Table XI. Symptoms were promptly relieved, and for two days his condition remained good. On the third day there were unmistakable signs of toxemia. The wound was in bad condition on account of great abdominal distention, and since the animal was practically moribund, he was sacrificed. At autopsy the large obstructed loop was found enormously distended and there were areas of beginning gangrene along the antimesenteric border. There was no peritonitis or other complication. The chemical findings are given in Table XI.

It is apparent in Table XI, that Dog 30 developed symptoms of hypochloremia only on the fifth day. This fall in chlorids is less rapid than we have seen in animals with simple obstruction, yet in this animal the whole small bowel was converted into an isolated loop filled with toxic fluids. The difference is due, no doubt, to the fact that his intestinal lumen was not blocked. In spite of his vomiting, a part of his stomach secretion passed on into the large bowel. His symptoms on the fifth day were relieved promptly by a hypodermoclysis of 2 per cent salt solution. Three days later, though his blood chlorids remained above the normal level, a fatal toxemia

developed as a result of damage to the wall by overdistention and strangulation. Previous to that time the intact mucosa had prevented the absorption of these toxins.

TABLE XI.

(Obstructed loop; duodenum anastomosed to ileum; water, *ad lib.*, by mouth; treatment as indicated in remarks.)

Remarks.	Day.	Mg. per 100 cc. blood.			Vomitus and urine.	
		Urea nitrogen.	Total nonprotein nitrogen.	NaCl.	Quantity, cc.	Grams.
No treatment	0	15.6	47.6	465		
No treatment	1	11.6	38.5	449	860	2.5
No treatment	2	16.6	39.7	425	1160	2.8
No treatment	4	15.6	51.3	359	1540	2.8
1000 cc. 2 per cent NaCl	5 10 P.M. .	34.1	68.9	321	750	1.4
1000 cc. 1 per cent NaCl	6	16.4	57.0	643	1310	3.3
	8	10.8	37.0	736	4860	14.5
						4.8*
	Total . .	...	...	...	...	32.1

* Washings from pen.

TABLE XII.

(Dog. 39. Obstruction of the duodenum; treatment as indicated in remarks.)

Remarks.	Day.	Mg. per 100 cc. blood.			Vomitus and urine.	
		Urea nitrogen.	Total nonprotein nitrogen.	NaCl.	Quantity, cc.	Grams.
1000 cc. 1 per cent NaCl*	0 . . .	9.4	37.9	531		
1000 cc. 1 per cent NaCl*	1 . . .	3.0	28.9	490	1360	12.12
1000 cc. 1 per cent NaCl*	2 . . .	9.6	37.7	457	980	8.50
1000 cc. 1 per cent NaCl*	3 . . .	9.8	18.9	506	460	2.15
1000 cc. 1 per cent NaCl*	4 . . .	14.8	42.5	507	715	6.44
No food; water, salt	6 . . .	16.4	36.6	543	1250	11.80
No food; water, salt	8 . . .	19.4	48.0	523	240	0.30
No food; water, salt	10 . . .	23.5	46.5	523	450	3.10
No food; water, salt	12 . . .	46.4	69.7	490	890	9.80
						5.00†
	Total . .	...	...	...	...	59.21

* Hypodermically.
† Washings from pen.

We believe that in acute simple obstruction, experimentally produced, the actual course is exaggerated by the absorption of toxins through the damaged tissues in the inverted stump of the bowel. The two dogs of Foster and Hausler,[5] to which we have

previously referred, demonstrate this fact. Dog 39 (Table XII) of our series was obstructed at the duodenum and allowed water *ad lib.* for five days. During this time he received 5000 cc. of a 1 per cent solution of sodium chlorid by hypodermoclysis. Thereafter all food, water, and salt were withheld. The dog continued in good condition until the twelfth day, dying, apparently, of inanition. Autopsy showed uncomplicated simple obstruction.

Though this dog did not live sufficiently long to furnish a striking demonstration, the results are in keeping with those of Foster and Hausler. If hypochloremia and dehydration are prevented for the critical period of the first five days, the animal, with simple occlusion of the intestinal lumen, may then exist throughout the period of inanition without food, water or salt. The loss of chlorids by vomiting under such conditions will be slight because the starving stomach secretes very little hydrochloric acid.

From a careful analysis of our results it becomes evident that death in acute simple obstruction is not due to toxemia. We have no evidence that a high level of blood chlorids prevents death from an existing toxemia and we see no reason for assuming a specific detoxifying action by sodium chlorid. The hypodermic administration of sodium chlorid solution has a specific therapeutic value in acute intestinal obstruction in that it overcomes the hypochloremia and the dehydration, both of which are lethal factors in this condition.

4. *The relationship between hypochloremia and the terminal increase in nonprotein nitrogen is not definite.* We have found that a marked fall in blood chlorids is always followed by a rapid increase in the concentration of the nitrogenous elements. In pointing to this relationship Haden and Orr have assumed it to be a definite indication that the obstructed bowel brings about a toxemia which fundamentally involves the chlorids. In our experience, however, this increase has often occurred in dogs with a normal blood chlorid level. The truth of this will be apparent from a study of the tables.

It will be observed in Tables VIII and IX, that animals, receiving large quantities of fluid by hypodermoclysis, show even at death very little accumulation of nitrogen in the blood; but animals, in which dehydration is allowed to occur show the increase in spite of normal blood chlorids. We have tried a number of experiments in an effort to separate these two factors. Dog 25 constitutes one experiment of this type.

Dog 25.—Ileum was obstructed 12 inches above the cecum and the distal segment was brought up into an enterostomy wound. The dog was allowed water, *ad lib.*, and at frequent intervals given an enteroclysis of tap water. By this means 800 to 1200 cc. of water daily was given into the bowel below the obstruction. The dog vomited freely, but remained in good condition for five days. On the sixth day he was markedly dehydrated and in tetany. Autopsy on this day showed distention of the whole

lower bowel and discoloration of the terminal foot of the ileum. There were no other complications.

TABLE XIII.

(Dog 25. Obstruction of the ileum with enterostomy into distal segment. Water by enteroclysis; no salt.)

Remarks.	Day.	Mg. per 100 cc. blood.			Vomitus and urine.	
		Urea nitrogen.	Total nonprotein nitrogen.	NaCl.	Quantity, cc.	NaCl, gm.
Good condition for five days	0	10.5	35.7	497		
	1	6.2	22.2	480	1320	4.55
	2	3.2	28.8	462	1830	0.55
	3	4.9	31.4	439	2420	0.42
	4	8.6	36.4	363	1370	1.12
	5	12.2	40.8	363	1290	2.18
	6	16.4	71.4	295	690	1.61
						4.16*
	Total	...	...	...	...	14.59

* Washings from pen.

This animal was one in which we devoted much effort toward the placing of fluid in the lower bowel where absorption might take place Dehydration was not marked till after the chlorids were greatly reduced. In this dog the increase in nonprotein nitrogen was relatively slight. The actual degree to which dehydration will ordinarily occur in obstructed animals allowed water *ad lib.* by mouth is shown in Table XIV.

TABLE XIV.

(Dog 52. Obstructed at mid-duodenum; water, *ad lib.*; no other treatment.)

Day.	Mg. per 100 cc. bood.			Blood.		Vomitus.		Urine.
	Urea nitrogen.	Total nonprotein nitrogen.	NaCl.	R. B. C.	Moisture.	Quantity, cc.	NaCl, gm.	
0	10.5	37.7	436	7,900,000	76.9			
1	5.6	31.9	436	8,900,000	73.8	690	4.2	
2	44.4	52.6	345	10,100,000	69.4	3370	4.9	
3	54.2	173.9	329	13,800,000	65.2	4450	2.8	
Total	...	...	...	...	...	...	11.9	

We have found it practically impossible to maintain the water balance in a dog with a marked degree of hypochloremia. It is

certain that the obstructed animal becomes dehydrated in spite of taking large quantities of water by mouth, and this dehydration becomes absolute as the chlorid level falls. In this state the excretion of urine is practically *nil* and we believe this the chief explanation of the rapid terminal increase in blood nitrogen.

In support of our views on this effect of dehydration we offer the findings in two dogs (Nos. 29 and 27).

Dogs 29 and 27.—Both were starved and caused to vomit twice daily by the hypodermic injection of apomorphin. One of them, Dog 29, was allowed, just previous to the administration of apomorphin, a limited quantity of water. From the other, Dog 27, all water was withheld.

TABLE XV.

(Starvation; vomiting induced twice daily by apomorphin.)

Remarks.	Day.	Mg. per 100 cc. blood.			Vomitus and urine.	
		Urea nitrogen.	Total nonprotein nitrogen.	NaCl.	Quantity, cc.	NaCl, gm.
Dog 29 (water in limited quantities)	0	16.2	71.8	504		
	2	9.1	39.7	490	940	2.50
	4	13.3	38.0	452	1290	2.20
	5	21.9	40.0	415	460	0.97
	6	16.5	43.5	407	110	0.18
	8	15.3	48.0	393	215	0.41
	10	17.9	43.0	408	140	0.28
	20	20.5	48.4	421	1530	2.00
Released	26	7.7	52.4	442	660	0.76
Dog 27 (no water)	0	12.8	33.3	530		
	1	12.6	31.9	530	680	3.42
	2	15.6	41.4	483	300	1.37
	3	13.2	46.1	492	220	0.60
	4	21.2	70.5	514	130	0.50
	5	29.3	106.8	515	116	0.20
Died	6	37.8	135.0	520	120	0.90

In neither of these animals did vomiting produce a large output of chlorids or a marked reduction of blood chlorids. Obviously vomiting which is not excessive and not associated with obstruction of the intestine will bring about no permanent disturbance in the secretion and reabsorption of chlorids. In Dog 29, which was allowed water, there was an appreciable fall in the blood chlorids but there was no nitrogenous accumulation in the blood when the dog was released on the twenty-sixth day. Dog 27, with no change in chlorids, died in six days and showed the rise in nonprotein nitrogen which we have found to occur always in fatal dehydration. Our findings indicate that the relationship which appears to exist between hypochloremia and the blood nitrogen increase of acute

intestinal obstruction is explained best on the basis of dehydration. A profound reduction of blood chlorids rapidly intensifies the already existing dehydration; there results a marked impairment of kidney function and a rapid accumulation of nonprotein nitrogen in the blood. This increase may also be due in part to increased tissue destruction from dehydration.

Early in our efforts to differentiate the factors of salt and water we verified the fact reported by Haden and Orr[4] that the hypodermic administration of water alone to an obstructed dog causes death sooner than no treatment whatsoever. This apparently astonishing fact was made more readily understandable when we discovered a similar administration of water to a normal dog to be rapidly fatal. Later we made a more careful study of this observation, and two such animals are reported herewith.

TABLE XVI.

(Dogs. 53 and 54. No water by mouth; hypodermic administration of distilled water as indicated in the remarks.)

Remarks.	Day.	Mg. per 100 cc. blood.			Blood.		Urine.		
		Urea nitrogen.	Total nonprotein nitrogen.	NaCl.	R. B. C.	Moisture, per cent.	Quantity, cc.	NaCl, gm.	Total nonprotein nitrogen, gm.
Dog 53 (distilled water)									
500 cc.	0 . .	15.8	44.3	490	6,900,000	78.9			
500 cc.	1 . .	8.1	32.4	468	6,000,000	79.2	365	0.27	4.73
500 cc.	2 . .	8.5	34.8	445	6,100,000	80.4	380	0.43	6.27
1000 cc.	3 . .	7.7	33.9	480	5,100,000	81.2	295	0.14	5.61
500 cc.	4 . .	9.8	29.9	490	4,800,000	82.4	650	0.31	6.50
Died	5 . .	51.2	62.5	430	...	85.2	50	0.05	0.60
Dog 54 (distilled water)									
1500 cc.	0 . .	10.7	45.9	513	7,000,000	79.8			
1500 cc.	1 . .	25.7	74.1	435	...	....	395	2.05	6.17
Died	2 . .	45.1	96.8	356	...	72.3	110	0.56	2.26

The exact mechanism of death from the administration of water is not clear. There is marked hemolysis of the red cells and this may be the explanation. The points which we wish to emphasize at this time are the lowered excretion of urine and the rapid terminal increase in blood nitrogen which resulted. This mechanism operated more rapidly in Dog 54, which received the large injections of water. It is interesting to note that this animal showed a reduction of blood chlorids which cannot be explained by his output. In this case the

chlorids have been drawn rapidly into the water-logged subcutaneous tissue. Unfortunately a second red cell count was not obtained on this animal but the determination of the total moisture in the blood showed an actual dehydration in the face of more than 2000 cc. of excess water in the subcutaneous tissue.

We regard this as a striking indication that a normal water and salt balance is essential in maintaining the kidney function as well as the entire metabolism of the body. The administration of salt alone is of no value if water is withheld. The parenteral administration of water alone is fatal.

Conclusions. 1. In acute simple obstruction of the small intestine where the bowel wall remains intact, death is not due to toxemia. The lethal factors are dehydration, reduction of blood chlorids by vomiting, and starvation. Administration of sodium chlorid and water by hypodermoclysis or any method which preserves the salt and water balance, will prolong life through the period of starvation.

2. In acute strangulation of the bowel the factor of toxemia is added. Treatment with sodium chlorid and water does not prevent death from this toxemia.

3. The increase in the nonprotein nitrogen of the blood appears to result chiefly from dehydration and a rapid reduction of kidney function. Hypochloremia is an important factor in this mechanism. It is also possible that hypochloremia and dehydration cause increased tissue destruction which adds to the nitrogenous increase.

4. For these reasons, the administration of physiologic sodium chlorid, by hypodermoclysis or intravenous transfusion, will be a valuable procedure in the treatment of intestinal obstruction and gastric tetany.

5. Since strangulation of the bowel occurs in most cases of obstruction, the limitations of the treatment are obvious.

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CLINICAL CAUSES AND DIAGNOSTIC AND PROGNOSTIC SIGNIFICANCE OF JAUNDICE.*

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Herbert Spencer says in one of his books, I think in *First Principles,* that mankind in its progress passes through three stages, the unanimity of the ignorant, the disagreement of the inquiring, the unanimity of the wise. Upon most questions in medicine we are still in the first stage, upon many in the second, upon none in the third. It was while thinking about jaundice that this expressive dictum of Herbert Spencer came to my mind. Up to a very recent period, as time goes, we were in comfortable agreement that jaundice was twofold, obstructive and toxic; the former due to gross obstruction of the outflow of the bile, the latter due to excessive destruction of red cells and consequently greater manufacture of bile by the obliging liver—all jaundice was therefore hepatogenous. The second period of our progress was not long in coming. It was shown by Virchow and others that a substance identical with bilirubin could be formed from extravasated blood outside of the liver. This led many to the conviction that bile was made both in the liver and outside of the liver. When at a later period, however, Minkowsky and Naunyn showed in experiments on birds that after the removal of the liver bile was no longer formed bilogenic monopoly was again restored to the liver.

Then came Aschoff and his pupil McNee,[1] and demonstrated, or seemed to demonstrate, that bile production was the property of certain large endothelial cells widely scattered through the body and identical with the stellate cells of Kupffer in the liver. To these endothelial cells found in the liver and in the spleen, in the lymph nodes, bone marrow, and so forth, Aschoff gave the name of reticuloendothelial system, and to this system he and his followers ascribe the property either of making bilirubin out of disintegrated or dead red cells or of preparing such cells for conversion into bilirubin by the liver.

Whipple and Hooper afterward showed that in the dog whose liver had been excluded from the circulation bile pigment was still formed and appeared in the blood.

Among the last and most important investigations in this field are those of Mann, Bollman, and Magath,[2] of the Mayo Clinic, who succeeded in extirpating the liver from dogs and keeping the animals alive for from twenty-four to thirty-six hours, a longevity never before attained. In such anhepatic dogs they found that

* Part of Symposium on Jaundice before the American Gastro-Enterological Association, May 5, 1926; containing also a report of some cases of epidemic jaundice.

bilirubin continued to be formed. Their observations were soon confirmed by Rich[3] and Makino.[4]

But scarcely had the work of Mann, Bollman and Magath been published when the conclusions drawn from it were challenged by Melchior, Rosenthal and Licht,[5] of Breslau. Repeating in general the technique of Mann and Magath, they tested the bile-forming power of the hepatectomized dogs with toluylendiamine and phenylhydrazine, which in control dogs produced marked icterus. They found that after the removal of the liver no appreciable icterus followed the injection of the poisons.*

As the matter stands today, insofar at least as the experimental evidence is concerned, no definite proof has been brought that bile is chiefly formed outside of the liver, in the so-called reticuloendothelial system, or of the fact, a corollary of the first, that the liver is merely an excretory organ for bile made elsewhere, as the kidney is for urea, with the formation of which it is in nowise concerned.

Nevertheless, I am inclined to believe, on clinical grounds, that bile can be formed extrahepatically. I have seen jaundice in cases of large fatty liver, the acute yellow hypertrophy of Rolleston, in which under the microscope scarcely an intact polygonal cell remained. The sections had all the appearances of areolar fatty tissue and could be recognized as of liver origin only by the presence of bile ducts.

Perhaps one more point should be mentioned in support of the theory of Aschoff and McNee and other recent experimenters as to the formation of bile outside of the liver, namely, the fact that van den Bergh and Gansslen, Zipperlen and Schüz[6] have found more bile pigment in the blood of the splenic vein than in that of the splenic artery, the spleen being as we know one of the most important constituents of the reticuloendothelial system.

I have gone into these few details because in the obscure field of clinical jaundice every datum of scientific research bearing upon the probable seat of bile formation is helpful to a better understanding.

The Clinical Causes of Jaundice. The classification proposed by van den Bergh into mechanic and dynamic is, in the main, satisfactory but perhaps a little too rigid. McNee has lately suggested a modification which is not unlike that of older writers and which helps I think to clarify the subject. McNee, an ardent reticulo-

* Aschoff, in a recent article (Klin. Wchnschr., 1926, 5, 1260) published after the present paper was written, takes issue with the Breslau experimenters and insists that their researches do not disprove the observations and conclusions of Mann and Magath. As regards the nondevelopment of jaundice in hepatectomized dogs after toluylendiamin and phenylhydrazin injections, Aschoff is of the opinion that the repeated glucose injections necessary to keep the dogs alive, may have had a share in preventing icterus. In any event the work of Mann and Magath proves the intravascular formation of bile pigment outside of the liver cell.

endothelialist, distinguishes: (*a*) Obstructive hepatic jaundice; (*b*) toxic and infectious hepatic jaundice; (*c*) hemolytic jaundice.

(*a*) OBSTRUCTIVE HEPATIC JAUNDICE. The clinical causes of obstructive hepatic jaundice, mechanical jaundice, are, in the main, the following:

1. Obstruction by stone or other foreign body in the common bile duct. This is one of the most frequent and most easily understood types of jaundice. Before the introduction of the van den Bergh test it was supposed to occur in about 10 per cent of cases of gall stone—at least, that was the surgeon's figures. I found it more frequent when, instead of asking only about the color of the skin, I also inquired as to the color of the urine.

The van den Bergh test has shown the great frequency of moderate bilirubinemia in many cases of biliary colic in which there is no visible jaundice and no choluria.

2. Through tumor of the bile ducts or of the head of the pancreas; also through pressure upon the ducts by large glands, by aneurysm of the hepatic artery, and so forth.

3. Through stricture of the duct as a result of scar formation.

4. Through inflammation of the mucosa of the duct with the formation of a mucous plug. This is the commonly accepted explanation for so-called catarrhal jaundice; however, no one it seems has ever found such a plug in acute catarrhal jaundice. More probably we are dealing in catarrhal jaundice with a cholangitis and mild hepatitis, or with acute swelling of the head of the pancreas analogous to mumps.

5. Through traction on the bile ducts by a floating kidney.

6. Through injuries—cutting of the bile ducts during operation. Jaundice under these conditions appears almost immediately, is permanent painless, but accompanied by intolerable itching, thus simulating the jaundice due to malignant obstruction.

7. Passive congestion of the liver in chronic heart failure. I am placing this in the group of obstructive jaundice although the mechanism of congestive jaundice is by no means clear. The obstruction of the ducts if it exists, is intrahepatic.

8. Cirrhosis of the liver. Here, too, whatever obstruction exists is intrahepatic, but other factors cannot be ruled out.

9. Carcinoma of the liver with intrahepatic or extrahepatic pressure.

In many cases of what appears to be purely mechanical or obstructive jaundice, for example, that due to a stone blocking the common duct, the liver is the seat of degenerative and inflammatory changes, of a hepatitis which may become a not easily evaluated factor both in the jaundice and in the general clinical picture.

(*b*) TOXIC AND INFECTIOUS HEPATIC JAUNDICE. This group comprises types of jaundice in which there is no gross mechanical obstruction in the extrahepatic ducts, barring an occasional excep-

tion to which I shall refer. Bile is present in the urine and in the feces. By the van den Bergh test the blood serum is said to give a delayed direct as well as a negative direct reaction (biphasic reaction, McNee).

Illustrations of this type of jaundice are:

1. *Weil's Disease.* This is now known as Spirochetosis icterohemorrhagica or leptospirosis. The disease became prominent as a clinical entity during the World War, which brought confirmation of the finding of the Leptospira icteroides originally discovered by Japanese observers. A number of true cases of spirochetosis have been reported in this country, among them 2 by Sailer.[7]

The disease sets in with chill, headache and prostration; occasionally the onset is gradual. Nausea, vomiting, abdominal and muscular pains, jaundice and fever complete the picture. Sometimes in bad cases a peculiar odor manifests itself. The liver is enlarged; the spleen not constantly.

The causative parasite normally lives in the wild rat; it is highly pathogenic for guinea pigs and can be kept alive and virulent in them for an astounding number of generations. It is present in human blood until about the seventh day of the disease and in the urine up to the fortieth day or longer. It should be looked for in dark-field illumination.

Immune bodies appear in the blood of patients and can be produced experimentally in animals so that both cure and prophylaxis in times of epidemic may become feasible.

2. *Infectious Jaundice, Nonspirochetal.* This as a rule is a mild type of jaundice. It is most common in children, and has of late years prevailed in widely scattered sections of this country. After an incubation period of from eight to ten days the disease sets in abruptly with fever, constipation and abdominal pain. Jaundice appears in four or five days or later—up to the twentieth day—and lasts for from seven to ten days, although it may disappear in a few hours or continue for six weeks.

The disease resembles acute catarrhal jaundice, indeed sporadic cases would undoubtedly be so diagnosed. Except for a milder course and absence of mortality, it is similar to Weil's disease, but the most careful search by Blumer, Wadsworth and Noguchi has failed to show any leptospira.

During the last few weeks we had a small outbreak of epidemic jaundice in Philadelphia. The 3 following cases occurred in one family:

Case Reports. CASE I.—P. D., aged thirteen years, was seized on the evening of April 13, 1926, with high fever and headache. The fever continued on the next day and nausea appeared. On the following day there was no fever but persistent nausea and some vomiting, with a crop of hives and much itching. On April 17 the eyeballs were yellow. The stools were pale but not putty colored; the urine contained considerable bile. There

was a slight enlargement of the liver, not of the spleen, and no abdominal tenderness.

CASE II.—S. D., aged twelve years, started on April 15, 1926, two days after her sister, with similar but milder symptoms. Her jaundice was slight although bile was readily demonstrated in the urine. When last seen, on May 2, there was still a faint tinge to the conjunctiva.

CASE III.—E. D., aged fifteen years, a third sister, was taken ill suddenly on April 19, 1926, four days after the second case, with no other symptom than fever (up to 104° F.) which continued for forty hours. On April 25, after she had been well four days, but still in bed, she became distinctly jaundiced and had pronounced general itching. There was also some vomiting.

It is interesting that having had routine examinations of the urine made in all three cases, bile was detected in the third patient's urine before the color of the eyeballs attracted attention.

In another case, also a young girl, which I did not see, but about which I was consulted, careful search was made for leptospira by Dr. Lynch, of the Pepper Laboratory, with negative results.

Such cases as those here described are in the beginning usually called grippe or influenza—often abdominal influenza—during the period of apparently causeless fever, nausea and vomiting. The subsequent discovery of jaundice is considered a sequel or a complication. I believe the whole process is a unitary disease due to some obscure transmissible infection which with the modern technique should not elude us for long.

While epidemic jaundice is a mild disease, it seems to bear a relation to acute yellow atrophy or acute degenerative hepatitis, as is shown by the following case:

CASE IV.—Dr. A. E. F., aged fifty-two years, a man in perfect health, was seized with jaundice, which in the course of two weeks became very intense. There was no pain at any time, only great prostration. The urine was black and the stools in the beginning were clay colored. When I first saw the patient, I concluded, not finding a palpable gall bladder, that I was dealing with one of those rare cases of silent stone or with a toxic hepatitis. Two days after my visit to him in his home town, he was brought to the Hospital of the University of Pennsylvania. He had a deep canary color, no fever, no tenderness and was apathetic, almost stuporous. The liver was not enlarged, perhaps it was a trifle smaller than normal; the spleen was not palpable. A somewhat striking feature was a peculiar body odor like that of fresh laboratory meat broth. Two days later he died in coma, our diagnosis being acute degenerative hepatitis. Autopsy showed complete freedom from disease on the part of the gall bladder and bile ducts but advanced degeneration of the liver. Both during life and after death careful search was made for spirochetes, but with negative results.

Now, there is in connection with this case a most interesting and suggestive fact which I ascertained prior to the man's death. Dur-

ing the few weeks before he fell ill, there had been an epidemic outbreak of jaundice in his community. He had attended from 18 to 20 cases, 5 of them being in one household. One cannot escape the belief that an infection was at work and that the doctor had received through his multiple contacts such an intensive dose of the poison that he developed what is comparable to an acute yellow atrophy of the liver.

I am trying to obtain some rats from the place where the jaundice has prevailed, but if the observations of Blumer and other investigators are borne out, our results will be negative.

3. *The Jaundice of Infectious Diseases.* Typhoid fever, pneumonia, septicemia, and so forth.

As a rule, the jaundice of pneumonia is a mild complication, but in rare instances it is severe and darkens the prognosis greatly. The sputum in the grave cases is a bright green color due to biliverdin. If one may use the van den Bergh reaction as a basis, the jaundice of pneumonia is in part due to an active hemolysis and in part to a toxic hepatitis.

4. *Toxic Jaundice.* Particularly that due to arsphenamin, chloroform, and so forth.

Much discussion has arisen as to whether the jaundice occurring after arsphenamin injections is syphilitic, that is, due to the Treponema pallidum or to gummatous lesions or to a toxic effect of the arsenic. If to either of the first two one might be inclined to push the arsphenamin; if to the last, nothing would be more harmful (Gordon and Feldman[8]). Blood bilirubin studies have shown that in certain cases the bilirubin content is increased when arsphenamin is given, long before any icterus is manifested externally. If the use of the drug is continued the bilirubinemia becomes more marked and finally, the threshold being passed, jaundice appears. It is due to a degenerative hepatitis which is best combated with glucose. If the van den Bergh test is regularly made in cases receiving the arsenicals the drug will be discontinued and glucose will be given as soon as the icterus index begins to mount and before severe liver damage has taken place (Gerrard[9]).

5. *Postoperative Jaundice.* I have already spoken of this as a possible consequence of trauma to the bile ducts during operation, but there is yet another type of postoperative jaundice—that in which there is an infective cholangitis or a septic thrombophlebitis of the portal vein. This type of jaundice is most frequent as a sequel of operations on cases of suppurative appendicitis and possesses a rather well-defined clinical physiognomy. Jaundice sets in a few days after operation, early in the development of the infection. (It can occur also in cases of appendicitis not operated upon.) Fever is present with chilly sensations, high leukocytosis, tenderness over the liver and localized edema. Lassitude, anorexia and emaciation are striking symptoms. The patients often remark

that "they are too tired to sleep." The Roentgen ray is of value in the diagnosis.

(*c*) HEMOLYTIC JAUNDICE. The term hemolytic jaundice* (icteroanemia) connotes a jaundice due to blood destruction and not to primary disease of the liver cells or any part of the liver. That at least is the meaning given to the term by the majority of French writers and by Minkowski, a German pioneer in this field. On the other hand, Naunyn and his followers, while attributing the jaundice to excessive blood destruction, believe that excessive amounts of pigment made in the liver cause the formation of thrombi in the bile capillaries. On that basis the jaundice would be the result of an intrahepatic obstruction. However, the newer researches on the origin of bile pigment strongly point to the possibility, as indicated in an earlier part of this paper, of an extrahepatic source for bile pigment, though perhaps not the only source. It is therefore probable that hemolytic jaundice is independent of obstruction of the bile capillaries.†

The blood destruction occurs chiefly in the spleen, liver, lymph nodes and bone marrow; but with respect to some of the conditions belonging under the head of hemolytic jaundice we have little knowledge of the place of blood destruction.

Two types of hemolytic jaundice are recognized: (*a*) The acquired type (Hayem-Widal); (*b*) the congenital or familial (cholémie familiale) (Chauffard-Minkowski). In both, far greater amounts than the threshold value of 4 units of bile pigment may be present in the blood without bile appearing in the urine—hence the synonym, acholuric jaundice. In most cases the bile is excreted as urobilin in increased amounts in the feces and also in the urine.

A number of features are common to both types:

1. There is a chronic jaundice, with the presence of bile pigment in the blood serum, but without bile in the urine (acholuric jaundice).
2. The signs of biliary obstruction are absent—there is no itching, no bradycardia, no clay-colored stools.
3. There are no bile salts in the blood.
4. Anemia is common to both types, but is more marked in the acquired, reaching at times as low a figure as 1,000,000 red cells.

* For a full discussion of this subject see Pearce, Krumbhaar and Frazier (The Spleen and Anemia, Philadelphia and London, 1918) and Meulengracht (Der chronische hereditäre hämolytische Ikterus, Leipzig, 1922).

† Dr. I. S. Ravdin calls my attention to an interesting statement by Riolanus, Jr., indicating that as far back as the seventeenth century a distinction was made between obstructive and nonobstructive jaundice. Riolanus (A Sure Guide or the Best and Nearest Way to Physick and Chirurgery, translated by Nicolas Culpepper, 1691) says: "When I see in an extremely yellow jaundice the whole skin infected with choler and that the urine dye cloths yellow, the stools being in the meantime whitish, and when I see in another sort of jaundice both urine and stools yellow, this confirms to me that there are two forms of choler and several ways for the expurgation of them."

5. The spleen is enlarged and firm.

6. Urobilinuria, an indication of blood destruction, is present.

7. Fragility of the red cells. This sign, first pointed out by Chauffard, is found in both types but is more marked in the congenital or familial than is the acquired. Normally, hemolysis in hypotonic salt solution begins at 0.42; in hemolytic jaundice it begins even as high as 0.6.

Blood regeneration is evidenced by an increase of reticulocytes.

8. Splenectomy is usually curative.

While the cases viewed in a large way fall into two groups, congenital or familial and acquired, the differences are scarcely fundamental and there are many borderline cases, as, for example, congenital cases with negative family history. Such cases are perhaps better classified with the acquired type.

Gall stones are quite common in familial or congenital hemolytic jaundice, but seem to bear no etiologic relation to the jaundice. In some cases, as pointed out in an admirable paper by Dutton,[10] crises occur during which symptoms of obstructive jaundice are added to the clinical picture. These crises are attributed by Dutton to a heightened activity of the neuromuscular reflex apparatus of the bile passages (see also Hopkins[11]).

In the acquired type acute exacerbations with deepening jaundice are frequent.[12] The acquired cases as a rule also present a severer clinical picture than the congenital. The latter, in Chauffard's words, are often more icteric than sick. A number of German writers[13] have called attention to the frequent coexistence of tower skull (Turmschädel) with hemolytic jaundice.

One may place under the head of acquired hemolytic jaundice, the icterus found in pernicious anemia and allied conditions in which the van den Bergh test shows increased values of the icterus index but in which there is no choluria.

Pathogenesis. The fundamental fault in hemolytic jaundice is either some lesion of the blood, such as might be called a dystrophy of the red cells, or an anomaly of the spleen that endows it with an exaggerated hemolytic activity. Since splenectomy is a curative measure, the latter hypothesis seems more reasonable. The spleen of hemolytic jaundice is not alone spodogenous, as it is in health, but it also destroys red cells in increased numbers and prepares others for destruction.

Difficult to explain on the lienal theory, however, is the fact that after the removal of the spleen the osmotic resistance of the red blood corpuscles to hypotonic salt solution sometimes remains as before, or does not return completely to normal.

Familial hemolytic icterus behaves in its hereditary transmission as a dominant character.

Icterus Neonatorum. This is a type of hemolytic jaundice due to rapid blood destruction. It occurs in about 50 per cent of

infants. The blood gives a positive indirect but negative direct van den Bergh reaction.

A rare example is the familial type of jaundice of the newborn, a grave disease occurring less often in the children of the first and second pregnancies than in those of later birth. Those that recover often show permanent cerebral or cerebellar defects.

Dissociated Icterus. French writers, and Hoover and Blankenhorn in this country, have called attention to dissociated icterus, that is, one in which bile salts and bile pigment are separate and do not occur together in the blood or urine. They recognize: (*a*) An hepatic dissociated icterus in which bile salts and bile pigments are separately present in the plasma as the result of separate hepatic excretion into the blood; (*b*) a renal dissociated icterus in which the bile pigment alone is present in the plasma due to renal excretion of the bile salts. The subject is one requiring further investigation.

General Features of Jaundice. 1. Yellowish discoloration of the skin, of the mucous membranes and of the deeper tissues is the most striking feature of jaundice. It is to be looked for first in the conjunctiva, and in colored races on the inside of the lower lip, the blood being pressed out with a glass slide.

The color varies from a light lemon or canary yellow to light or dark orange or olive brown. The darkest types are seen in the most chronic cases of obstructive jaundice, although a dark color of the skin is not necessarily proof of a high degree of bilirubinemia. Tears, cartilage, nerves and muscle tissue do not show staining. Pneumonic sputum in cases of jaundice is often light green in color due to oxydized bilirubin.

2. Itching of the skin is one of the most distressing of all jaundice symptoms. It occurs in obstructive not in hemolytic or toxic jaundice. It may precede the icterus—preicteric itching—hence it is probably not due to the bile pigment, but to bile salts or other constituents of the bile. In bad cases of itching the skin is more or less covered with scratch marks and often shows infection.

Surgical drainage or cholecystoenterostomy almost immediately puts a stop to the itching long before the color has faded from the skin; this is another point in favor of the view that the itching is not due to the bile pigment.

Xanthoma occasionally forms in long-standing jaundice.

Some cases of jaundice have a peculiar odor like that of fresh meat broth. This is particularly true of icterus gravis and of spirochetal jaundice.

The blood serum normally is slightly bile stained, the amount of bilirubin present, as measured by the delicate van den Bergh test, being from 0.5 to 2 mg. in 100 cc. of blood (1 to 2,000,000 to 500,000). A false augmentation of color may be produced by the presence of considerable amounts of carotin or lutein derived from the diet.

I shall not give the details of the van den Bergh test.* It will suffice here to say that in this test Ehrlich's diazo reagent is added to the blood serum. Normally the bilirubin of the blood gives the so-called delayed direct or indirect reaction, while that in the bile gives the immediate direct reaction. In the case of the blood, the immediate development of a bluish-violet color indicates, in van den Bergh's opinion, the presence of an excess of normal bilirubin and is to be interpreted as signifying obstructive jaundice with the resorption of normally formed bile from the liver. If the addition of alcohol to the serum-diazo mixture causes a deepening of the color, or the appearance of the characteristic color when there had not been any before, the reaction, called positive indirect, is interpreted as being due to bile pigment that has not been acted upon by the polygonal cells of the liver, and hence the test is significant of hemolytic jaundice. Whether this sharp differentiation drawn by van den Bergh and by McNee is correct has not been proved; indeed the most recent researches throw doubt upon it.

Icterus Index. The icterus index, a term first used by Stetten, is based upon a colorimetric comparison of the depth of color of the blood serum and a standard solution of potassium bichromate, 1 to 10,000, as proposed by Meulengracht.† The depth of color is expressed by a number called the icterus index, the normal index ranging from 4 to 6. Bernheim has arranged the following table expressing the range of the icterus index.

Zone of hypobilirubinemia	2.3 to 4
Normal zone	4 to 6
Zone of latent jaundice	6 to 15
Frank jaundice	Above 15

All cases with an index above 15 show jaundice, but a yellow skin and sclera may persist for some days after the index goes below 15, because bilirubin disappears more rapidly from the blood than from the other tissues.

Value of the Icterus Index. By means of the index it is possible to detect latent jaundice, that is, a bilirubinemia without clinical icterus. In cases of colicky pains of indefinite nature the presence of latent jaundice points to a biliary origin. The index may be used to follow the changes in the degree of jaundice in patients with frank icterus. As pointed out by Snell,[14] the test helps in the discovery of hepatic congestion in early myocardial failure, in the

* The following are among the more important references to this subject: Van den Bergh: Presse méd., 1921, **29**, 441. Van den Bergh and Snapper: Deutsch. Arch. f. klin. Med., 1913, vol. **110**. Meulengracht: Arch. Int. Med., 1925, **35**, 214. Stetten: Ann. Surg., 1922, **76**, 191. Bernheim: J. Am. Med. Assn., 1924, **82**, 291; Arch. Path. and Lab. Med., 1926, **1**, 747. Ravdin: Am. J. Med. Sci., 1925, **169**, 850; Surg. Clin. North America, February, 1926. Greene, Snell and Walters: Arch. Int. Med., 1925, **36**, 248. Greene, McVicar, Rowntree and Walters: Arch. Int. Med., 1925, **36**, 418, 542.

† This test has been advantageously modified by Bernheim, who has substituted a glass standard for the 1 to 10,000 potassium bichromate solution.

differentiation of hemolytic from other anemias, and in the early demonstration of jaundice due to obstruction in the common duct.

Bernheim has shown that in gastric ulcer there is a normal bilirubinemia, while in duodenal ulcer (except in cases with hemorrhage) there is a hyperbilirubinemia. The retention of bile may be due to an extending duodenitis or to a certain degree of hyperglobulia which has been found not infrequently in ulcer of the duodenum. In diabetes mellitus the icterus index is high—the lowest index in 41 diabetic patients was 7.5; the highest, 15, the average, 10. The severe cases showed the highest indexes.

Bernheim has pointed out a possible use of the icterus index in the prognosis of pneumonia. No case with a normal bilirubinemia ended fatally. Although death did not occur in all cases showing hyperbilirubinemia, in no fatal case was this condition absent. As in many instances it is not possible to foretell the outcome from the clinical aspect, it is desirable to make further tests of the icterus index in the hope that it may prove of use both in prognosis and in the choice of therapeutic measures.

Hypobilirubinemia, revealed by the icterus index, is found in cases of secondary anemia not due to blood destruction but caused by hemorrhage or by lessened production—conditions in which less hemoglobin is liberated. In Bernheim's series every case of secondary anemia with a red cell count below 3,000,000 showed hypobilirubinemia.

Carotinemia. This condition, described by Hess and Myers, and to which I have already referred, is due to the prolonged use of carrots and other vegetables, fruits, eggs, and other foodstuffs, containing yellow pigments (lutein, xanthophyll, carotin). It produces a high icterus index—Greene and his associates found it as high as 26. By chemical tests, either the van den Bergh or the Meulengracht, it is readily shown that the actual amount of bilirubin is not above normal. A feature differentiating carotinemia from icterus is its tendency to be more prominent on the thicker epithelium, such as the palms and soles.

I might add further that the indirect reaction of van den Bergh has helped in the detection of latent jaundice in pernicious anemia and dibothriocephalus anemia and, as pointed out on a previous page, in the recognition of latent jaundice due to the toxic action of arsphenamin.

One more blood change might be mentioned—Thewlis and Middleton[15] have demonstrated the existence of a leukopenia in uncomplicated cases of catarrhal jaundice. They show that sometimes the leukopenia precedes the appearance of the jaundice.

The Urine in Jaundice. In obstructive jaundice the urine is bile stained, but often the intensity of staining varies in different voidings for reasons that are hard to find. In hemolytic jaundice the urine as a rule is not bile stained (acholuric jaundice).

Urobilin or urobilinogen appears in the urine in cases of jaundice in which obstruction, if present, is not total, so that some bile can get into the intestines and be acted upon by bacteria. Hence its determination has been suggested as a test to distinguish catarrhal jaundice from that due to carcinoma of the head of the pancreas or the common bile duct, as in the usual case of carcinoma no bile whatever enteres the intestine, therefore none can be transformed into urobilin (Wallace and Diamond[16]).

In cases of severe or of long-standing jaundice albumin and bile-stained tubocasts are present in the urine. Leucin and tyrosin appear in the urine in acute yellow atrophy. They were not found in the case of fatal icterus gravis reported in an earlier part of this paper.

The Feces. The clay or putty-colored stools of jaundice due to extrahepatic obstruction are well known. Such stools are seen at times in cases of toxic jaundice, evidently through an associated intrahepatic obstruction. In cancer of the head of the pancreas the feces are pale and shiny, due in part to unabsorbed fat and in part to the absence of bile; they look like buckwheat-flour dough and spread out thinly on the floor of the vessel.

Other Effects of Jaundice. In true hemolytic jaundice the fragility of the red blood cells is increased. While normally the breaking up of the cells occurs at between 0.44 to 0.34 per cent saline solution, in hemolytic icterus it begins at 0.6 or even 0.7 and is complete at 0.5 per cent.

A *lessened coagulability* has long been known to occur in chronic jaundice and has been much dreaded by surgeons as a source of hemorrhage. Its causes are not well understood. Although calcium injections prevent postoperative hemorrhage in jaundice cases, there appears to be no special loss of calcium in the blood. It may be, as suggested by Snell, that in jaundice the calcium and the bilirubin enter into some sort of combination which virtually entails a lessened calcium content.

Metabolic Effects of Jaundice. Most common are subnormal temperature and slow pulse. Emaciation may develop rapidly in obstructive jaundice, even in the absence of malignant disease. I have seen extreme loss of flesh in nonmalignant obstruction.

Nervous Disturbances. The most distressing of these is itching, which in stone or in malignant obstruction may become more unbearable than pain. It robs the patient of sleep and contributes to his rapid decline. Irritability and mental depression may occur even in mild types of jaundice, while in toxic jaundice there may be muttering or agitated delirium, coma or convulsions.

Diagnosis. In approaching the subject of the diagnosis of jaundice, or rather of its causative condition, we may with profit follow the advice of Deaver and ask: "Is the jaundice painless or is it painful?"

Painful jaundice is usually due to mechanical causes, especially to stone, to cholecystitis or to cholangitis. In rare cases the jaundice of calculus is painless—the so-called silent stone. It is not necessary that there should be successive attacks of colic—one definite painful seizure is of great help in the diagnosis of calculous obstruction.

If the jaundice is painless, the possibilities are many—with clay-colored stools and choluria, the suspicion falls on the pancreas or some other nearby structure. The most valuable diagnostic feature of jaundice due to the disease of the pancreas is a large gall bladder (Courvoisier sign). By gentle palpation the gall bladder may be felt; often it can be seen to move under the skin during respiration if the examiner will sit at the patient's side, with his eyes almost on a level with the abdomen.

Glycosuria favors the diagnosis of pancreatic disease, but does not permit exclusion of disease of the bile passages or liver.

I have thought that itching appeared earlier in malignant than in calculous obstruction; and as I have stated, the itching may be preicteric.

The icterus index is of value. A variable icterus index speaks in favor of stone, a constant or increasing figure is most common in extraductal or noncalculous obstruction.

Referring once more to the large gall bladder, it should be stated that, while most common in cancer of the head of the pancreas, it is also found in carcinoma of the papilla. Mention should also be made of a possible source of error due to the occurrence of the so-called Riedel's lobe, an elongated linguate projection of the right lobe of the liver, sometimes found in gall stones. It may readily be attributed to tumor or a large gall bladder.

I shall not refer to the various functional liver tests which may possibly prove of value in the final differentiation of the causes of jaundice. At present the tests give us information of the state of the liver rather than of the causes of jaundice. Such information is, however, of value in forming a comprehensive judgment of the patient as a surgical risk. When carried to a greater state of perfection they will undoubtedly become part of our routine preoperative study of jaundice cases.

Prognosis. The prognosis of jaundice can be as little stated in a few words as the prognosis of fever. It depends on the cause, on the resistance of the patient and very often on the intelligence of the medical adviser and on the skill of the surgeon.

In the hemolytic forms of jaundice, barring the graver anemias and hemolytic poisons, the prognosis is favorable. Cure is often achieved by splenectomy.

Regarding the other types of jaundice, I would say that no form of obstructive jaundice should ever be taken lightly. It is always

possible for a jaundice of mild beginning to become grave, as the case of the doctor I have cited above so well illustrates.

Jaundice may affect the outcome of the operation done for its relief. One should hesitate to promise early recovery in any case of jaundice no matter how simple the contemplated operation may be. In some elderly persons—analogous to what happens at times to the kidneys after prostatectomy—a postoperative hepatic insufficiency develops. There is but little drainage of bile, the appetite is in abeyance, the patient is exceedingly languid and seems incapable of making a fight for his recovery. Death may ensue in three or four weeks despite active treatment. It is probable that not only the liver but also the pancreas has a share in the disastrous outcome.

Under the use of calcium chlorid intravenously by the Walters method hemorrhage has been practically eliminated as a danger after operation upon jaundice cases. The prophylactic and postoperative use of glucose solution has lessened the incidence of liver disfunction or nonfunction. Nevertheless, I am of the opinion that in the presence of jaundice it behooves the surgeon to limit his interference to the essential minimum. I have seen lives sacrificed through the operator's eagerness to correct all pathologic defects in the abdomen. It is probable that the liver function tests will eventually make operations safer.

The prognosis is also influenced by the state of the other organs, particularly of the kidney and of the heart. A closer relationship exists between the kidney and the liver than is appreciated or is explainable in the light of our present knowledge. As for the heart, the prognosis is not so vitally affected by its condition if that be not too serious. In fact when the history permits the decision that the bile duct tract disease antedates the heart trouble, then we may conjecture that the gall bladder disease may be responsible for the disease of the heart and that operation may not only cure the disease of the biliary passages but also that of the heart as well.

In no other circumstances is it so important to take a comprehensive view of a patient's powers of resistance as in cases of jaundice that require operation. The laboratory tests, as I have stated above, are of value not only with respect to the jaundice itself, but also in throwing light on the functional capacity of the liver, kidneys, heart and pancreas. But in the last analysis the best judgment is reached by him who has had a large clinical experience and uses it wisely.

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CHOLECYSTOGRAPHY AND LYON–MELTZER TEST IN A PATIENT WITH A CONGENITALLY ABSENT GALL BLADDER.

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This article is brought before the medical profession, not so much on account of the infrequency of the congenitally absent gall bladder as for its substantiation of the value of cholecystography and for the light it throws on the source of Lyon's B bile. There are also included observations on the diabetic's postoperative intraäbdominal adhesions on differences of medical and surgical procedure and on the way to proceed in clearing up questionable diagnosis of perinephritis and subdiaphragmatic abscess.

Case Report. G. S. a female, aged forty-eight years, born in Russia, was admitted to the Medical Service of Unity Hospital, December 5, 1924. Her chief complaint on admission was pain in the right upper abdomen and cramps. Since 1922 she had had several attacks of severe pain in the right hypochrondrium which radiated toward the back. These attacks increased in severity until the beginning of November, 1924, when the patient was operated upon at the Brownsville and East New York Hospital, for cholelithiasis, but after a thorough search by two competent surgeons no gall bladder was found and a normal appendix was removed. Two weeks following operation pain in abdomen and cramps returned. Abdominal pain is not influenced by meals, but aggravated by coughing. The patient desires to urinate when attacks of pain come on. Cramplike nature of pain later disappeared, and there is no nausea or vomiting. Pains in back, especially right side posterior (December 12, 1924). Patient on admission also complained of nocturia three or four times.

Family History. This has no bearing on case.

Past History. The patient had measles, pneumonia and bronchitis, but had no operation, with the exception of the one five

weeks ago mentioned above. Menstrual and marital histories are essentially negative.

Physical Examination. The patient is undernourished. The mucous membranes are red. There are areas of pigmentation on the face and there are numerous irregular pigmented spots present all over the body, but no pigmentation of conjunctiva or mucous membrane of mouth. The teeth are in poor shape; bridgework is present, but no pyorrhea. The tongue is coated. The eyes react to light and accommodation; the pupils are equal. The mastoid is not tender. The ears and nose are negative. The thyroid is palpable. The epitrochlear, axillary and inguinal glands are not enlarged. The mammary glands are normal. The heart, with the exception of a moderate tachycardia, is negative. The lungs are negative. Tenderness is present at right trapezius, subscapular and right lumbar region. Right Murphy sign is positive. The abdomen is prominent—slight umbilical hernia (size of a quarter) is present; no dullness in flanks; no sign of fluid is present. Liver: Upper border in fourth space, lower border at crest of ilium; it is perfectly smooth; edge is sharply defined, hard and goes upward, until it is lost beneath the costal cartilage. Left side is not enlarged. It moves with respiration. The spleen is not enlarged. The kidneys are not tender nor palpable. The upper extremities are negative. The lower extremities—no involvement of bones, joints or muscles. No Babinski is present and all reflexes are normal.

The patient was in the hospital for three and a half weeks with normal temperature and pulse varying from 74 to 86 and respirations varying from 22 to 24. The systolic pressure averaged 130 and the diastolic averaged 80.

Laboratory Examinations. Numerous urine examinations were made and sugar was found varying from 1.1 to 5 per cent, with a daily output of 5.5 to 58 gm.; the daily output varied from 1200 to 2000 cc. Acetone and diacetic acid were also present. A few pus cells were found. After the nineteenth day from date of admission numerous examinations showed absolutely negative urine.

The blood showed the following:

BLOOD.

	Nov. 8, 1924.	Nov. 11, 1924.	Dec. 13, 1924.	Dec. 15, 1924.	Jan. 3, 1925.
Red blood cells	...	...	4,000,000		
Hemoglobin	...	...	75%		
Color index	...	...	1.0		
Coagulation time	...	...	6 minutes		
White blood cells	15,600	13,200	13,800	14,400	10,200
Polymorphonuclears	78%	79%	76%	74%	38%
Eosinophils	1%	0	0	...	0
Lymphocytes	18%	19%	24%	26%	49%
Macrocytes and transitionals	3%	2%	0	...	12%
Mastocytes	0	0	0	...	1

The blood culture of December 18 proved sterile. The Wassermann test of the blood was negative Blood chemistry: December 8: Blood sugar, 250 mg. per 100 cc. December 13: Blood sugar, 300 mg. per 100 cc.; urea nitrogen. 12 mg. December 16: Blood sugar, 20 mg. per 100 cc.; urea nitrogen, 16 mg ; CO_2, 46; creatinin, 1.2 mg. Gastric contents, 50 cc.: December 13: Total acidity, 30; free HCl, 16; no lactic acid; microscopically, starch granules and no blood. The feces showed, on examination of five different stools, no parasites, no blood, normal color, consistency and odor, with somewhat increased amount of fat. The Schmidt test for pancreatic function was positive.

January 3, 1925: A perinephritic puncture was done, and only a little blood was obtained, which on cytologic and bacteriologic examinations proved negative.

The Lyon-Meltzer test of December 18, 1924, showed the typical three-colored specimen: (*a*) 10 cc. of a golden yellow, (*b*) 50 cc. of dark green with much mucus and (*c*) a few cubic centimeters of a light yellowish fluid. This fluid obtained through the duodenal tube gave chemically all the tests for bile, showed a few red blood cells and leukocytes and a moderate number of bile-stained epithelial cells. No crystals were found. All sorts of contaminating bacteria were present.

Cystoscopic Examination (Dr. Goldfader). This showed bladder and ureter orifices normal; bladder urine clear. Roentgen ray catheters, 6F., inserted into each kidney pelvis without obstruction. Phthalein intramuscularly appears from each kidney in seven minutes. Specimens of urine from each kidney clear. Pyelogram and ureterogram of right kidney pelvis and ureter, with 10 cc. of 15 per cent sodium iodid for pelvis, 4.5 cc. of same for ureter and 2 cc. of 25 per cent argyrol into left kidney pelvis.

The urine obtained by cystoscope shows: Right kidney: Numerous red blood cells, occasional white blood cells and few cuboidal epithelial cells. Left kidney: Few amorphous urates and occasional red blood cells Bladder: Numerous red blood cells (about 10 per high-power field). Cultures of 3 different specimens were sterile.

Roentgen Ray Examination (Dr. Strahl). The pyelogram shows no evidence of urinary calculi. The opaque catheters can be seen in the pelvis of both kidneys. Pyelogram is fairly good size. The ureterogram shows a slight dilatation at the juncture of the lower middle third and intermittent contractions at the lower one-third.

The fluoroscopic examination does not reveal any displacement of the right diaphragm or the presence of any intrathoracic fluid. The Roentgen ray picture shows an universal haziness in the abdominal cavity, more marked on the right side and suggesting disease in the right hypochondriac region.

Roentgen ray of the gastro-intestinal system shows the stomach

is not ptosed. Very active peristalsis, prepyloric filling defect. This filling defect is due to adhesions between the stomach and liver. Six-hour examination shows no gastric residue; the meal is in the terminal ileum; twenty-four-hour examination shows the meal in the large bowel; forty-eight-hour examination shows meal also in large bowel. Diagnosis: Intraäbdominal adhesions. Gastrointestinal tract is negative.

The patient was given intravenously 5.5 gm. of tetrabromphthalein. She had a severe reaction, consisting of intense headache, chill, palpatation, vomiting and prostration. Cholecystography revealed no gall bladder shadow.

Report of Brownsville and East New York Hospital. (A personal conversation with the surgeons who operated upon this patient.) After exposure of the gastrohepatic omentum, and a most thorough search for the gall bladder, it proved to be congenitally absent. The common and hepatic ducts could be plainly traced, but there was no sign of the cystic duct. The walls of the duct were smooth and showed no knobs, thickening or dilatation. A large Riedel lobe of the lower liver was found. After a most thorough search of the entire abdomen, with negative results, a normal appendix and a piece of liver tissue were removed for pathologic examination. The liver showed microscopically fatty infiltration of liver cells with swelling of endothelium of bile ducts.

Urine Examinations. (Six examinations, before and after operation.) No sugar was found at any examination, and the urine was normal in every respect.

Blood Counts. On two occasions the blood showed: (1) Leukocytes, 9000; polymorphonuclears, 84; lymphocytes, 16. (2) Leukocytes, 8000; polymorphonuclears, 79; lymphocytes, 21.

Final Diagnosis. Riedel's lobe of liver; choleduodenitis; pancreatitis; diabetes.

Discussion. This patient, with a congenitally absent gall bladder, and having a Riedel lobe of liver, evidently had an infection which started in the common bile duct and ascended into the biliary ducts and ultimately involved the liver cells, as shown on microscopic pathology of the piece of liver removed at operation. This pathology explains the subjective and objective symptoms presented by the patient which led the surgeon to perform a gall bladder operation. The infection then traveled down the duct of Wirsung and involved the pancreas, particularly the islands of Langerhans, which gave rise to the symptoms of a rather severe diabetes. It is interesting to note how the biliary and diabetic symptoms completely disappears with the subsidence of the infection. The patient is perfectly well today on a regular diet.

I wonder what percentage of diabetes is due to an infection starting in the common bile duct and involving the pancreas secondarily by means of the duct of Wirsung or by the circulation! Whether,

in diabetes we would get better results if we paid more attention to the eradication of biliary infection, as was done in this case, by means of nonsurgical drainage, autogenous vaccines and so forth. I believe that the severe backache which made us suspect a perinephritic abscess, was really due to involvement of the pancreas.

Although no intraäbdominal adhesions were present at the time of operation, they were quite marked shortly afterward, as evidenced roentgenographically. It is surprising how quickly and extensively these adhesions will form after prolonged intravisceral manipulations.

The pain and tenderness in the right lumbar region was so marked that in consultation with the genitourinary surgeons they favored the diagnosis of a kidney lesion, especially a perinephritic abscess. A complete urine examination cystoscopy, pyelography and a perirenal aspiration excluded any renal disturbance and saved the patient a useless operation. In a similar manner a right subdiaphragmatic abscess, which at one time was considered as a strong diagnostic possibility, on account of the severe pain and tenderness in that region, was excluded by aspiration, Roentgen ray pictures and especially fluoroscopy. This observation certainly lends additional confidence in the value of the employment of scientific investigation before operation to save the patients needless surgery.

There are many cases of congenitally absent gall bladder reported in the literature, and more cases are reported where the gall bladder is intrahepatic. L. C. Knox has encountered 2 cases of congenitally absent gall bladder in 2000 autopsies. These conditions are certainly not incompatible with life or even good health. These patients, however, are not infrequently susceptible to biliary disease and are often operated upon for cholecystitis or cholelithiasis, as was our patient. The question might be raised whether this patient did not have an intrahepatic gall bladder. Before cholecystography only an autopsy could have given a positive answer. But now we know that the live shadow cannot obliterate the shadow of the gall bladder filled with bile and tetraiodobromphenolphthalein. With the usual technique employed in cholecystography, the gall bladder shadow is revealed in spite of the fact that it is covered by the thickness of the whole liver, for the gall bladder lies not in front of the liver, but behind it. If the gall bladder were situated intrahepatically only part of this liver thickness would be in front of the gall bladder, and since the shadow of the whole liver thickness fails to obliterate the gall bladder, the shadow of only a part of the liver thickness would certainly not obliterate it.

Summary. This is the first reported case with a congenitally absent gall bladder on which cholecystography and the Lyon-Meltzer test were performed.

While most observers believe that the dark (B) bile comes from the gall bladder, there are some who doubt this. Observations

made on cholecystectomized man and animals do not approach the normal physiology of these biliary passages and therefore are not conclusive.

Here we have congenital absence of the gall bladder, and yet the patient presents, on the duodenal injection of magnesium sulphate, the three typical specimens of bile, including the dark (B) bile, which is supposed to come from the gall bladder.

There is only one conclusion to draw from this, and that is that the B specimen does not always come from the gall bladder, if it ever does.

A FINGER PUNCTURE METHOD FOR THE BLOOD SEDIMENTATION TEST.

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PHILADELPHIA.

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Not long after the blood sedimentation test was shown to have clinical value, attempts were made to perfect a technique requiring a small quantity of blood so that venipuncture would not be necessary. This is in the direction of simplicity and is highly desirable, for venipuncture at best is not without possible danger. In stout individuals with hidden and inaccessible veins and in children, some procedure not requiring venipuncture is a necessity, if this test is to be of universal application.

I wish to present a technique which utilizes the graphic principle of presentation (Cutler[1]), but in which venipuncture is not essential. I call this technique the Pipette or Finger Puncture Method for the Graphic Presentation of the Blood Sedimentation Test in contrast to the Tube Method for the Graphic Presentation of the Blood Sedimentation Test in which venipuncture is essential. In the former a specially designed pipette is the all-essential apparatus, while in the latter it is a specially designed tube.

The details of the pipette method are as follows:

Apparatus Required. 1. A pipette, 2.5 mm. internal diameter with the stem graduated in 50 mm. divisions. The capacity of the graduated portion of the pipette is less than 0.3 cc., a quantity of blood easily obtained by puncture of the finger tip.

2. A metal spring attachment (Van Allen) for closing the bottom of the pipette after it is filled with blood.

3. A rack for holding sedimentation pipettes.

4. Small storage tubes, of about 1 cc. capacity in which the blood is collected and kept until ready for making observations.

5. Small rack for holding storage tubes.
6. A sharp lancet.
7. Sedimentation charts for recording observations.*

Procedure. 1. Select one of the fingers of the hand and carefully cleanse the distal phalanx with an alcohol sponge, rubbing briskly to induce hyperemia. It is sometimes of service to immerse the finger in hot water for a few minutes, expecially in anemic individuals or where the skin is thicker than usual.

2. Puncture distal phalanx on its palmar surface and toward either side. This insures an easier flow of blood.

3. Collect blood in storage tube until about half filled (0.5 cc.). The storage tube which must be clean and dry is first filled with 3 per cent sodium citrate solution and its contents emptied. The quantity of citrate solution clinging to the walls of the tube is sufficient to prevent clotting of blood. From time to time the finger tip and the rim of the storage tube should be wiped with the citrate

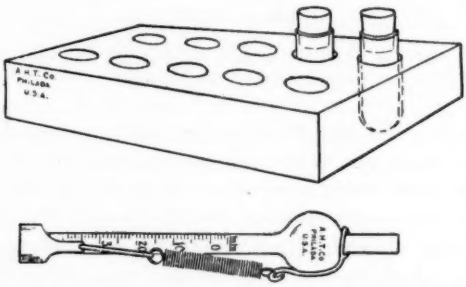

FIG. 1.—Storage tubes and rack. Sedimentation pipette with spring-sealing device (Van Allen) attached.

solution to remove possible clotted particles, and the tube shaken, as a further safeguard to prevent clotting. This is important. If clotting occurs the test must be repeated. In general the less the time consumed in obtaining the quantity of blood desired and the greater the ease with which the blood is obtained, the less the likelihood of the blood clotting and also the more accurate the result. I have not been able to obtain 0.5 cc. of blood from puncture of the finger tip without resorting to subsequent squeezing of the finger. Although there are objections to this procedure, for all practical purposes, as is evident from the results in the table and also in Fig. 3, if squeezing is done gently and systematically, dependable results will be obtained.

4. If samples of blood are to be obtained from several patients, place the storage tube in its rack and pay no more attention to it,

* These may be obtained from Charles M. Berkemeyer, Sellersville, Pa. The apparatus may be obtained from Arthur H. Thomas Company, Philadelphia, Pa.

until all the samples have been obtained. Cork each storage tube with a paraffin-coated cork to safeguard against accident.

5. When ready to make readings, (several hours may elapse with safety, after taking the samples of blood), shake each storage tube gently but thoroughly to insure uniform distribution of blood cells, for in many instances marked sedimentation may occur by the time one is ready to make readings.

6. Draw blood into the sedimentation pipette up to the zero graduation and attach spring cap to bottom of pipette. Here again certain details will prove of value. Draw the blood into the pipette by means of mouth suction on the rubber tube until the stem is filled with a *solid* column of blood, then holding the pipette in a horizontal position, remove the rubber tube and with pressure of the finger tip on the opening of the pipette, reduce the column of blood until the top is exactly at the zero mark.

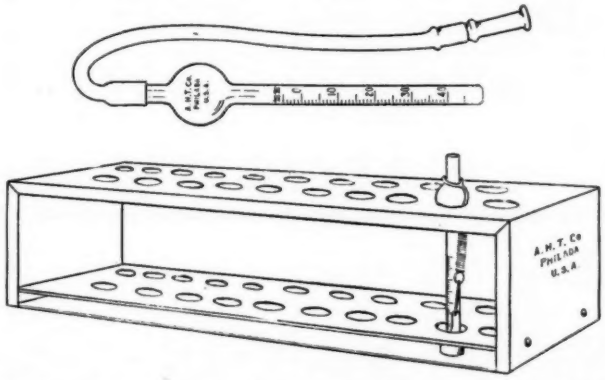

FIG. 2.—Sedimentation pipette and rack. The latter is constructed to provide complete visibility of each pipette during sedimentation.

7. Place the pipette in the sedimentation rack and determine the change in velocity by observing the position of the upper level of the sedimenting column of red blood cells every five minutes for one hour. These observations are recorded on the sedimentation charts, on which the horizontal lines represent the divisions on the stem of the pipette and the vertical lines the intervals of time. In this way a graph is traced which shows the position of the sedimenting column of red blood cells at any period of time during the first hour (see Fig. 3). The value of the sedimentation test is determined according to the path traversed by the red blood cells and depends upon the nature of the graph, sedimentation index and sedimentation time. All this has been fully described in a previous communication and reference should be made to that paper for clearer understanding. The purpose at present is simply to describe a new technique, not requiring venipuncture.

THE BLOOD SEDIMENTATION TEST IN PULMONARY TUBERCULOSIS.

Comparative Results of Tube and Pipette Methods, Both Tests Made Simultaneously upon Each Patient. Figures in First Line Opposite Case Number are for Tube Method, Serving as a Control, in Second Line for Pipette Method.

Case No.	Graph.				Sedimentation index, mm.	Sedimentation time, minutes.	Case No.	Graph.				Sedimentation index, mm.	Sedimentation time, minutes.
	Horizontal line.	Diagonal line.	Diagonal curve.	Vertical curve.				Horizontal line.	Diagonal line.	Diagonal curve.	Vertical curve.		
1	+ / +	...	...	...	1 / 2		22	...	+ / +	...	...	10 / 10.5	
2	+ / +	...	...	...	2 / 2.5		23	...	+ / +	...	...	11 / 10	
3	+ / +	...	...	...	2 / 2.5		24	...	+ / +	...	...	12 / 12	
4	+ / +	...	...	...	2.5 / 3		25	...	+ / +	...	...	13 / 13	
5	+ / +	...	...	...	2.5 / 2.5		26	...	+ / +	...	...	10 / 13	
6	+ / +	...	...	...	3 / 5.5		27	...	+ / +	...	...	13 / 14	
7	+ / +	...	...	...	3 / 1.5		28	...	+ / +	...	...	14.5 / 16.5	
8	+ / +	...	...	...	3 / 3		29	...	+ / +	...	...	15 / 14	
9	+ / +	...	...	...	4.5 / 4		30	...	+ / +	...	...	16 / 12	

9	+ / +	...	...	...	4.5 / 4	
10	+ / +				4 / 4	
11	+ / +	...	...	...	5.5 / 5	
12	+ / +	...	...	...	3.5 / 5	
13	+ / +	...	...	...	5 / 5	
14	+ / +	...	...	...	5.5 / 2	
15	+ / +	...	...	...	6 / 5.5	
16	+ / +	...	...	...	6.5 / 9.5	
17	+ / +	...	...	...	8 / 8	
18	+ / +	...	...	...	8 / 6	
19	+ / +	...	...	...	8 / 10	
20	+ / +	...	...	...	10 / 9.5	
21	+ / —	— / +	...	...	8 / 13	
30	...	+ / +	...	...	16 / 12	
31	...	+ / +	...	...	16 / 15	
32	...	+ / +	...	...	16 / 16	
33	...	+ / +	...	...	16 / 15	
34	...	+ / +	...	...	21 / 19	
35	...	+ / +	...	...	21 / 17	
36	...	+ / +	...	...	21.5 / 20.5	
37	...	+ / +	...	...	21.5 / 20.5	
38	...	+ / +	...	...	22 / 22	
39	...	+ / +	...	...	22 / 23	
40	...	+ / +	...	...	25 / 25	
41	...	+ / +	...	...	25 / 25	
42	...	+ / +	...	...	24.5 / 22	

BLOOD SEDIMENTATION TEST IN PULMONARY TUBERCULOSIS—(*Continued*)

Comparative Results of Tube and Pipette Methods, Both Tests Made Simultaneously upon Each Patient. Figures in First Line Opposite Case Number are for Tube Method, Serving as a Control, in Second Line for Pipette Method.

Case No.	Graph.				Sedimentation index, mm.	Sedimentation time, minutes.	Case No.	Graph.				Sedimentation index, mm.	Sedimentation time, minutes.
	Horizontal line.	Diagonal line.	Diagonal curve.	Vertical curve.				Horizontal line.	Diagonal line.	Diagonal curve.	Vertical curve.		
43	...	...	+ / +	...	19 / 20	60 / 60	53	...	...	+ / +	...	21.5 / 20.5	45 / 50
44	...	...	+ / +	...	24.5 / 26.5	60 / 60	54	...	...	+ / +	...	23 / 23	45 / 50
45	...	...	+ / +	...	27 / 27	60 / 55	55	...	...	+ / +	...	25 / 26	40 / 40
46	...	...	+ / +	...	27 / 27	60 / 60	56	...	...	+ / +	...	28 / 30	45 / 40
47	...	...	+ / +	...	27 / 27	60 / 60	57	...	...	+ / +	...	25 / 26	40 / 40
48	...	...	+ / +	...	21.5 / 22	55 / 55	58	...	...	+ / +	...	28.5 / 29	40 / 40
49	...	...	+ / +	...	20 / 24	55 / 55	59	...	...	+ / +	...	29.5 / 31	40 / 45
50	...	...	+ / +	...	24 / 25.5	50 / 50	60	...	...	+ / +	...	29.5 / 29	35 / 35
51	...	...	+ / +	...	26 / 26	50 / 50	61	...	...	...	+ / +	26 / 25	35 / 30
52	...	...	+ / +	...	26 / 26	50 / 55	62	...	...	...	+ / +	30 / 30	30 / 25

If one compares the pipette or finger puncture method with the tube or venipuncture method it becomes evident that the pipette method is the tube method on a smaller scale, requiring a quantity of blood which can be obtained by puncture of the finger tip and that that is the only essential difference. The manner of recording and interpreting the results is exactly the same.

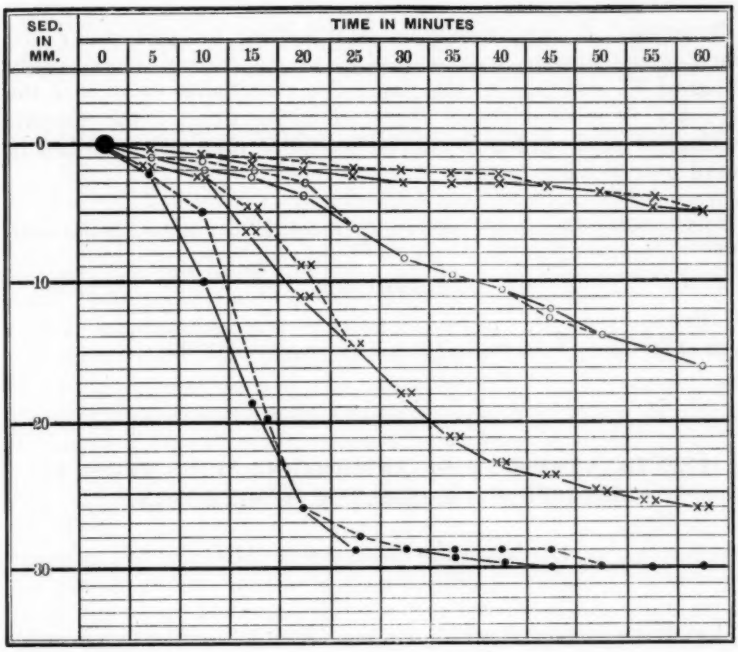

FIG. 3.—Comparison of graphs as obtained with pipette and tube methods.

x – – x – –
— x — x —
} Horizontal line (clinically healthy individual).

– – o – – o – –
— o — o —
} Diagonal line (clinically quiescent tuberculosis).

– – xx – – xx – –
— xx — xx —
} Diagonal curve (clinically slightly active tuberculosis).

– – · – – · – –
— · — · —
} Vertical curve (clinically markedly active tuberculosis).

– – – – – – – – Graph obtained with pipette method, requiring puncture of finger tip.

———— Graph obtained with tube method, requiring puncture of vein.

The table on pp. 690–692 shows the comparative results obtained by the tube method in which venipuncture is essential and by the pipette method in which venipuncture is not employed, the blood being obtained by puncture of the finger tip. Both tests were made

simultaneously upon each patient, the tube method serving as a control in each instance. All patients studied were afflicted with pulmonary tuberculosis. It will be noticed that the pipette method parallels the tube method very closely and that the differences that occur here and there are of minor importance and do not interfere with a practical interpretation of the result. The character of the graph which is the all essential feature of the graphic method is the same in both.

Summary. A new technique is described for performing the blood sedimentation test, requiring a quantity of blood easily obtained by puncture of the finger tip, thus doing away with the necessity of venipuncture. This technique utilizes the graphic method of presentation developed by the author and described in detail in a previous paper.

NOTE.—I wish to express my thanks to Dr. Harry J. White for his valuable assistance.

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THE TRANSMISSION OF PATHOLOGIC SIGNS FROM A DISEASED TO A HEALTHY HEMITHORAX.*

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THE transmission of pathologic signs from a diseased to a healthy lung is a well-known phenomenon, but the mechanism responsible for it is variable and in need of investigation. The mode of transmission may be extrapulmonic and intrapulmonic, or may be a combination of both. The extrapulmonic transmission may be conducted through the bony thoracic structures, the pleural membranes, pathologic products of the pleuræ, as adhesions attached to the chest wall, and effusions. In this category may also be included pneumothorax. The intrapulmonic transmission is conducted through the lower part of the trachea, the bronchi, and both lungs.

A. **The Extrapulmonic Mechanism.** 1. The tone of a vibrating tuning fork, applied to the teeth, can be heard over the skull, along the entire vertebral column, and even over both elbows of the examined individual. The thoracic bony structures have a distinct

* From the Tuberculosis Division of the Montefiore Hospital for Chronic Diseases and Bedford Hills Sanatorium.

conductive power. Sounds emanating at one point of the chest can be conveyed along the bony framework to another part. (Turban[1] and Barach[2]). The following observation may be cited as an example of the transmission of pathologic signs by means of the spinal column and the ribs toward the healthy side.

Case Reports.—CASE I.—(No. 8361.) The patient had undergone a thoracoplasty on the right side. The partially collapsed lung contains a tuberculous cavernous lesion and emits bronchocavernous breath sounds with an amphoric quality. In addition there are loud pleuritic creaks synchronous with the phases of breathing. The left lung presents no evidence of clinical activity and its roentgenogram is negative. The mediastinal shadow shows marked displacement to the right. However, very loud bronchocavernous breathing, almost amphoric in character, is heard over the vertebral column at the level of the fifth to the eighth vertebræ, and over the left lung posteriorly, beginning at the fifth costal interspace down to the eighth. Over the left supraspinous fossa there are audible dry crackles of a pleuritic character, not synchronous with the breath sounds. On a subsequent examination, two months later, the amphoric quality of the breathing was still present over the collapsed lung and over the healthy side. The pleuritic sounds had disappeared from both sides.

Due to the thoracoplasty, the collapsed lung on the right side was in direct contact with the spinal column. As a consequence, the bronchocavernous breath sounds emanating from the cavity in the right lung were transmitted by conduction to the vertebral column, and from here to the left transverse processes of the vertebræ and the left ribs. Hence, the pathologic breath sounds were heard over the vertebral column and the left side. In addition the bronchocavernous breathing was probably also transmitted through the intrapulmonic route—by means of the trachea and bronchi. As to the pleuritic creaks, the close mechanical relationship which exists between the costal pleura and the ribs suggests that the bony thoracic framework may have transmitted them from the diseased right, to the normal left, side.

2. In patients with pneumothorax in which a flaccid mediastinum and a collapsed lung yield to the pressure of the insufflated air, pathologic signs may be audible on the untreated hemithorax. The collapsed lung, being displaced beyond the midline of the sternum or the spinal column, is thus enabled to convey signs to the sound side.

CASE II.—(No. 8345.) The patient was receiving gas insufflations every two weeks into the left pleural space. Physical examination showed: Right lung: No discernible abnormalities. Left lung: Hyperresonance anteriorly and posteriorly; absent breathing anteriorly and very feeble breathing posteriorly. Moist râles posteriorly extending from the hilum region downward and toward the axillary line. No cardiac displacement.

Roentgenogram: Right, normal lung shadow; left, partially collapsed lung; apex and extreme base are adherent to the chest wall. Heart outline normal in size and position.

After the last insufflation, the physical examination revealed dextrocardia. In addition, there appeared a few moist râles near the right nipple and very many moist râles in the right intrascapular region. These râles were more intense over the spinal column, and became still louder when traced over the left hilum.

Fluoroscopy: The nonfixed portion of the left lung deviates together with the insufflated pleural space into the right hemithorax. There are pendulumlike oscillations of the entire mediastinum during the phases of breathing; on inspiration the right lung expands and pushes the mediastinum toward the left; on expiration the right lung contracts and simultaneously the left lung and the mediastinum move toward the right. The "to-and-fro" movement of the heart is especially marked, ranging from complete dextrocardia during expiration to almost normal sinistrocardia during inspiration.

One month later, after some of the insufflated air had been absorbed and the left lung had ceased to protrude into the untreated hemithorax, no râles could be elicited over the right lung.

Analyzing the clinical data, it is obvious that the moist râles which appeared over the right hemithorax after the last refill were due to the extreme displacement of the partially collapsed left lung and the mediastinum toward the right. The râles were thus directly conveyed from the left lung through the spinal column which acted as a conductor and through the right chest wall, posteriorly and anteriorly.

B. The Intrapulmonic Mechanism. If a tuning fork be set into vibration, and the prongs be inserted into the open mouth, the tone produced will not be of sufficient intensity to be transmitted through the thoracic structures to the chest wall. However, intense pulmonary râles are known to be reverberated in the trachea and heard orally. We may assume that pathologic sounds of sufficient intensity, originating in a diseased lung, will be conveyed by the trachea and bronchi to the opposite healthy side. Considering that most of the pathologic sounds produced in the chest are not sufficiently intense to be transmitted by the intrapulmonic route, the latter will assume a minor, and even insignificant rôle beside the more powerful conductive mechanism of the bony framework.

CASE III.—(No. 8238.) The patient shows an unusual improvement after a very acute and extensive unilateral caseous pneumonia. The left upper lobe is destroyed, leaving a cavity. The pleura over the left lung is thickened and the heart is drawn to the left by adhesions. There are constant râles of a bubbling character over this lung. The roentgenogam of the right lung is negative. The percussion sound over the right lung is normal, and the breath sounds appear on auscultation only a trifle sharper than normal. Large, moist râles are heard over the right upper lobe, however, both anteriorly and posteriorly, which vary in their intensity; at times they are altogether absent.

CASE IV.—(No. 7761.) There is evidence of a large cavity in the left lung. The mediastinal structures are drawn to the left. Roentgenography of the right side shows only a marked accentuation of the root markings. There is cavernous breathing over the left lung. Distant cavernous breath-

ing is also audible over the right upper lobe, posteriorly and anteriorly. This sign on the healthy side was occasionally absent.

Review of the Literature. The first reported pathologic sign transmitted from a diseased to a healthy lung is bronchial breathing in croupous pneumonia. Fenger,[3] in 1856, made the observation that in many patients with croupous pneumonia sharp bronchial breathing may be heard over the healthy side. The absence of consolidation on this side was checked up by postmortem examination. Sahli[4] writes: "In pneumonia, bronchial breathing is heard not only over the consolidated area, but also over the opposite healthy side in the neighborhood of the spinal column." Skoda[5] emphasized the resonating power of the bronchial structures made rigid through consolidation. Thus it becomes plausible that an immovable consolidated lung portion, while being in contact with the spinal column, may transmit the resonated or consonated bronchial breathing to the vertebræ and over the healthy lung by conduction.

The transmission of râles was detected in 1872 by Budde,[6] Turban,[1] in 1899, likewise reports the transmission of moist râles to the healthy contralateral side; the transmission of sibilant and sonorous râles from one side of the thorax to the exact opposite point on the other hemithorax; and in pneumothorax very feeble "metallic breathing" on the healthy side. Turban attributes these findings to the conductive power of the bony parts of the thorax.

Korány,[7] in 1897, noted in cases of pleural effusion a paravertebral triangular area of dullness on the healthy side near the base. Grocco,[8] in 1902, and Rauchfuss[9] made similar clinical observations. This paravertebral triangular area has since been designated by some as Grocco's triangle, by others as Rauchfuss' triangle. Baduel and Siciliano,[10] in 1904, offered the following explanation for the causation of the dull percussion note obtained in Grocco's triangle. The fluid lying against and passing anteriorly over the bodies of the vertebræ acts as a mute in suppressing the vibrations of the spine. This deadening of the resonance is appreciable beyond the median line over the area corresponding to the transverse processes and the mesial part of the ribs. The displacement of the mediastinum is an additional factor in producing the dull percussion note and may even compress the nondiseased lung.

Analogous to Grocco's triangle, Carpi,[11,12] in 1911, demonstrated in cases of pneumothorax a hyperphonetic zone on the contralateral side. This zone corresponds to the bulging of the pleural space at the posterior mediastinum produced by the tension of the gas. Carpi explains that the gas-distended space expands anteriorly over the midline of the spinal column so that with percussion of the spinal column and the adjacent chest wall, a resonant note is obtained, because this area will act as a resonator.

Carpi[13] also established in 1912 that patients with artificial pneumothorax presented râles transmitted to the healthy contralateral side. He recommended for comparative auscultation in such cases the double stethoscope as originally proposed by von Muralt.[14] He also claimed that the transmitted râles decreased as the air pressure was increased and disappeared completely when there was a complete collapse.

Heim and Jeanneret-Minkine[15] compared the lung status before and after the induction of pneumothorax in order to identify râles transmitted from the diseased to the healthy side.

Solomon[16] and Ameuille[17] emphasize the fact that transmitted signs occur chiefly at the posterior aspect of the chest. Solomon believes that transmitted râles are never heard in the axillary space.

Lindblom[18] reports 4 cases of pneumothorax in which râles were heard over the nontreated lung before insufflation; after air was introduced the râles diminished or disappeared. Solomon[16] illustrated with 5 cases that the induction of pneumothorax obliterated the original source of the abnormal signs, and therewith the transmitted sounds disappeared. Thus pneumothorax can be used for diagnostic purposes.

Genevrier and André-Robin[19] report, in 1922, an interesting case of right artificial pneumothorax in which the right apex was compressed against the spinal column; the râles from this apex were transmitted to the left apex. With a decrease in pressure the râles on the healthy side disappeared and became more audible on the diseased side.

Gendron,[20] in 1922, describes 1 case of partial pneumothorax with serofibrinous pleurisy in which on the healthy side the same pathologic signs were heard as over the diseased, even changed breath sounds and egophony. The sounds disappeared after refill. He claims that the fluid between the vertebral column and the noncollapsed portion of the lung conveyed the pathologic sounds. He mentions also the previously introduced theories for the transmission of pathologic signs; namely, that enlarged tracheobronchial lymph nodes and the vertebral column facilitate sound conduction.

Genevrier and Duval-Arnold[21] suggest the following differential diagnosis for the transmission of abnormal signs: On auscultation, transmitted pathologic sounds will be synchronous with those on the diseased side. They will be qualitatively similar, but not absolutely identical. The localization will not be exactly symmetrical. The most frequent site of origin will be near the spinal column. The transmitted sounds will be heard most often in the paravertebral area or in the supraspinous and infraspinous fossæ. Vocal fremitus, which will be heard increased only over the diseased side, is a good diagnostic help, as well as unilateral dullness on percussion. Roentgenologic examination is important. (The author would like to add that such examination is not necessarily always conclu-

sive, since early lesions may be clinically detected before the roentgenogram demonstrates them.) Diagnostic pneumothorax is not reliable because, while the insufflation may interfere with the conduction of the râles to the surface of the thorax on the treated side, it would not hinder the direct transmission of these râles to the untreated side.

In addition, the paradoxical phenomenon can be mentioned that physical signs may be transmitted from a clinically healthy to a diseased hemithorax. Clark, Hadley, and Chaplin,[22] in 1894, stated that in cases of fibroid disease of the lung and pleura, the resonant note usually elicited on the healthy side may be traced transgressing the midline, both along the sternum in front and the spine behind. Hamburger,[23] in 1906, detected in unilateral exudative pleurisy a resonant zone near the vertebral spine on the diseased side; and in the same year,[24] he also described a similar zone near the sternum on the diseased side in cases of pleurisy where the effusion extended anteriorly. He explains that during percussion of the affected hemithorax there are set up vibrations in the adjacent chest wall of the sound side, which, in turn, create a hyperresonant zone on the diseased side. Lillie[25] believes that the bulging of the emphysematous sound lung across the midline is the anatomic basis of the paravertebral resonant area on the diseased side. There is now under my observation a case (No. 8476) of unilateral pulmonary tuberculosis, presenting a fibroulcerative involvement of the entire left lung and thickening of the pleura. The roentgenogram shows a dense shadow occupying almost the entire left hemothorax; the mediastinum and heart are drawn to the left, and the right emphysematous lung protrudes over the midline. Percussion reveals an area of hyperresonance on the diseased side, adjacent to the vertebral column, which is especially pronounced at the base.

Summary. *A.* The following examples of transmission of pathologic signs have been noted:

1. Bronchocavernous breathing to the vertebral column and to the healthy lung posteriorly in a case of thoracoplasty.
2. Pleuritic creaks to the contralateral supraspinous fossa.
3. Moist râles to the anterior and posterior aspect of the opposite chest.
4. Cavernous breathing to the upper lobe of the healthy hemithorax, posteriorly and anteriorly.

B. An explanation for the mechanism of transmission is offered.

Conclusions. The transmission of pathologic signs from a diseased to a healthy lung is accomplished by means of two different mechanisms: (1) The extrapulmonic; (2) the intrapulmonic. They may act independently of each other, or in a combined manner.

While analyzing the pathologic states held responsible for the transmission of signs it must be borne in mind that secretions from a diseased lung may infrequently shift into the contralateral side,

creating temporary physical manifestations there. It must be remembered as well that certain nonpathologic conditions may be present in the nontuberculous side, such as muscle sounds, or definite pathologic changes, such as tumor, bronchiectases, etc., which may simulate transmitted signs.

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EARLY CRANIECTOMY AS A PREVENTIVE MEASURE IN OXYCEPHALY AND ALLIED CONDITIONS.

With Special Reference to the Prevention of Blindness.

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Premature synostosis of the cranial sutures, particularly of the coronal and sagittal, is a disorder which has extremely serious complications and sequelæ, notably, marked deformity of the face and head, increase of intracranial pressure and, in a very large proportion of cases, partial or complete loss of vision from optic atrophy. Operation for the condition has up to the present been performed only as a palliative measure after complications or sequelæ have developed and irreparable damage has occurred. For reasons to be discussed it is probable that the evil effects of synostosis are largely preventable by a suitable operation performed sufficiently early in life. Mehner,[1] in 1921, proposed "extirpation of the synostosed suture," but we find no record that his suggestion was ever carried out. In 1924 one of us,[2] unaware of Mehner's proposal, advocated the revival of the Lane-[3]Lannelongue[4] operation of linear craniectomy or craniotomy, which had for many years fallen into disrepute because it had been mistakenly used in the treatment of anencephalic microcephaly and other incurable forms of idiocy.* It was pointed out that in oxycephaly and allied conditions there is no primary brain defect, but that the deformity arises from mechanical interference with the growth of the brain by a relatively inexpansile skull, and that increased intracranial pressure and loss of vision occur as late sequelæ. The removal of ample strips of calvarium, if done during the period of rapid growth, might logically be expected to permit approximately normal development of the skull and thus prevent the serious consequences mentioned.

We now wish to present the case report of a child operated upon in 1924, who has been under close observation during the ensuing two years.

Case I.—Baby C, male, born on December 12, 1923, birth weight 7 pounds 8 ounces, was admitted, January 12, 1924.

* Jacobi (Med. Rec., 1894, 45, 609) said "If any cases be at all amenable to treatment by such an operation, they must be those of uncomplicated premature ossification of the sutures and fontanelles."

Family history: Father and mother are young and in good health. One previous pregnancy ended in abortion, cause not stated, December, 1922.

Birth was at full term, with head presentation; no instruments; no difficulty noted, but membranes are said to have ruptured five days before delivery. There was no asphyxia. Bottle feeding was begun at three days.

Present complaint: Feeding directions were desired.

FIG. 1.—May 6, 1924. Age, five months. There is slight asymmetry with prominence of the left temporal region; a rather wide interocular space; prominence of the forehead, marked backward and downward slope of the calvarial profile posterior to the bregma, prominence of the occiput, and marked bulging of the temporal veins on crying.

Physical examination: In other respects normal, the baby was found to have marked malformation of the skull. The frontal region was square and large, the anteroposterior diameter long. The parietal and occipital regions were flattened laterally and the occiput elongated, the whole posterior half of the calvarium giving the impression of being pinched in the transverse direction. The anterior fontanelle was triangular with the apex anteriorly, the angles continued with the metopic and coronal sutures which were wide open; the posterior border was almost a straight line, without a notch for the sagittal suture, which was apparently closed nearly to the posterior fontanelle and its line indicated by a bony ridge. There was no proptosis of the eyes. The temporal veins were prominent, especially on crying. No syndactylism or other malformation was present. Blood Wassermann test was negative.

Roentgenologic report: "The sagittal suture is ossified. Coronal, occipital and frontal sutures gaping."

Diagnosis: Premature synostosis of the sagittal suture; scaphocephaly.

By April 15, 1924, another examination showed several changes to have occurred. Definite asymmetry was now present. The right side of the forehead was more prominent than the left, the right parietal region more rounded and elevated than the left.

FIG. 2.—June 27, 1924. Age, six and a half months. Taken eight days after operation. The eyes show slight proptosis and the palpebral fissure is wide. The veins do not appear. The postbregmatic region is more rounded and elevated than before operation.

FIG. 3.—January 13, 1925. Age, thirteen months. The calvarial profile appears normal. The highest point of the skull is now at about the midparietal point instead of at the bregma, as before. The occiput is not prominent.

The forehead, as a whole, was more protuberant, the occiput less so. The fontanelle had greatly narrowed (about 0.6 by 3 cm.). The head was much broader in relation to its length than before. No proptosis was present and the eyegrounds were normal.

On June 17 the anterior fontanelle was practically closed. Bulg-

ing of the temporal regions and beginning proptosis were now present. The head was markedly brachycephalic. The temporal veins were very prominent. The fundi were normal.

Although in the roentgenogram the coronal sutures could be seen, the changes in the shape of the skull and the apparent closure of

FIG. 4.—July 2, 1925. Age, eighteen and a half months. A slight bulge of the left temporal region is still discernible. The profile appears normal. The interocular distance appears to be relatively less than in Fig. 1.

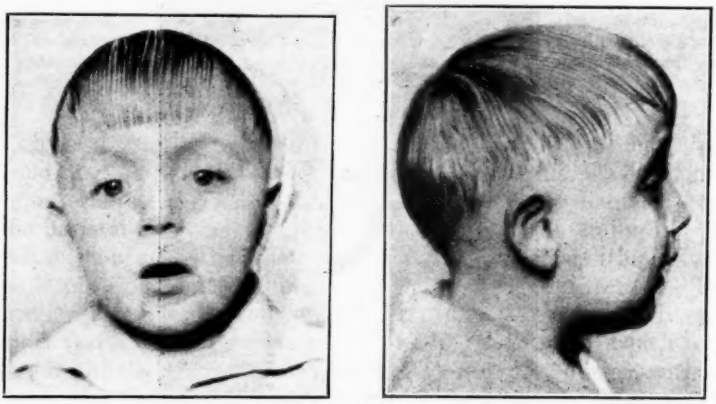

FIG. 5.—November 29, 1926. Aged, three years. The slight bulging of the left temporal region is the only remaining deformity. The child does not habitually hold the mouth open.

the fontanelle strongly suggested that these sutures were closing, the left perhaps more than the right. It was evident that there was an increasing maladjustment of the brain and brain case and possibly beginning increased intracranial pressure. After full discussion with his mother, it was decided to perform a linear craniectomy, which was done on June 19, 1924. The notes of the operation follow:

Operation by E. B. T., June 19, 1924: Linear craniectomy, under ether anesthesia. A transverse scalp incision was made between points 2 cm. above each external auditory meatus. The scalp was dissected backward to expose the upper portion of the lamboidal suture, and forward to expose the coronal sutures. The lamboidal and left coronal sutures were open; the sagittal and right coronal were closed. There was an open metopic suture. Two channels were cut in the cranial bones; the first was to the right of the sagittal suture and extended from the coronal to the lamboidal suture; the second lay posterior to the coronals, and extended from one squamo-parietal suture to the other. The channels were 1 cm. wide and included the overlying pericranium. A wick of rubber tissue was

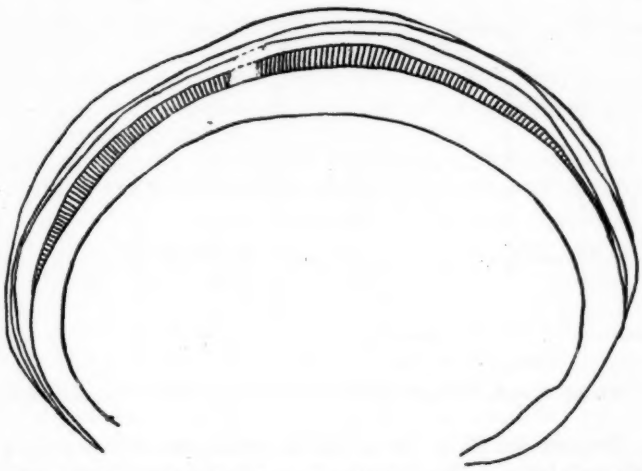

FIG. 6.—Superimposed tracings from the lateral roentgenograms of the skull dated January 14, June 18 (one day before operation), June 25 (six days after operation), August 12, October 21, 1924, and April 9, 1925. The shaded area represents the expansion of the skull occurring within the six days following operation.

passed through a stab wound over the posterior end of the sagittal craniectomy, and the scalp incision was closed with two layers of interrupted sutures.

Postoperative course: The drain and cutaneous sutures were removed on the third day. The wound healed cleanly. The child was dismissed from hospital on the seventh day.

Six days after the operation roentgenograms showed that the vertical diameter of the skull (sella to vertex) had increased about 4 mm.

By August 12 the proptosis had entirely disappeared, the forehead was less bulging and the temporal veins were less prominent. The anteroposterior craniectomy had widened to about 2.5 cm. at the new fontanelle, which pulsated and showed a normal crying impulse. The temporal bulging persisted, more on the left. Viewed from

above, the asymmetry was decidedly less marked. The mother was impressed with the child's improvement in appearance and behavior, stating that he appeared brighter, cried less and played more actively (indicating at least that the baby was making normal progress for his age). Tracings from the roentgenogram of this date shows growth of the skull in all directions, the brachycephaly being slightly more marked.

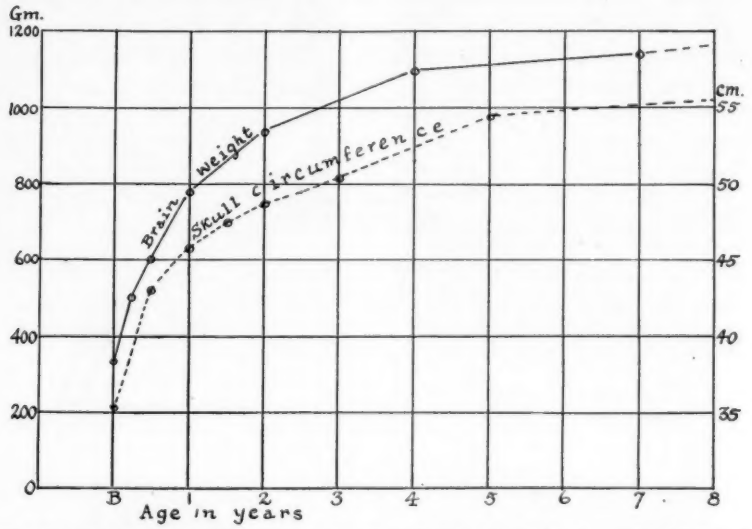

FIG. 7.—Graph showing the normal growth of skull and brain during early childhood.

By October 10, 1924, the artificial sutures were definitely filling in with new bone. The prominence of the forehead was less. The posterior portion of the skull had grown considerably, the anterior but little. No proptosis was present. The appearance was notably improved. The child was walking without support, could say a few words and had eight teeth.

By January 13, 1925 (age, thirteen months), the channels made in the skull had apparently closed. There was no striking change in the shape of the skull from that last noted.

By April 7, 1925, the head was apparently normal in shape and appearance. Mentally the child was "certainly normal," perhaps brighter than the average for his age. Plates at this time showed considerable growth of the skull to have taken place.

A more careful note on July 2, 1925, stated that slight bulging of the temporal fossæ and of the forehead could be detected and that the parietal dome was slightly flattened, but the appearance as a whole was not notably abnormal. The photographs bear out these statements. At nineteen months of age the child talked freely, forming short sentences, knew his alphabet and could count to ten.

Photographs and measurements in February, 1926, show a child of essentially normal appearance and development. On November 29, 1926, after the completion of our manuscript, the patient was again seen and photographed. He was then just under three years of age and two and a half years had elapsed since the operation. While a slight asymmetry of the head can be detected when his hair is flattened as it was for the photographs the configuration of face and skull is very nearly normal. His physical and mental progress continue to be excellent. No visual defects have developed.

Summary. This patient before operation showed a rapidly progressing deformity of the skull, due to synostosis of the sagittal suture, and later synostosis of one or both coronal sutures, with signs of beginning increase in intracranial pressure. The deformity, at first that of a simple scaphocephaly, had changed in the direction of oxycephaly. Following operation the shape and development of the head became approximately normal. The chief demonstrable benefit has been cosmetic. It is possible that blindness from optic atrophy has been avoided.

Comment. In this case it is probable that we have restored some, if not all, of the conditions necessary for the normal development of a skull which, already deformed by sutural synostosis, was likely to develop increasing deformity and widespread disturbance of the anatomic relationships, not only of the calvarium, but of the base, the orbit and the soft parts, possibly including the optic nerve. The results obtained then may be fairly regarded as of much more than simple cosmetic importance. In justification of our advocacy of preventive operation in similar cases and of linear craniectomy as the operation of choice, we wish to call attention to the frequency of visual impairment and to the pathologic conditions responsible for it.

Algyogyi[5, 6] in one place estimates the incidence of impaired vision at over one-third and in another at almost one-half of the cases of tower skull. Fifteen, or 71 per cent, of Mehner's[1] 21 cases showed it. Beyond doubt, many cases escape notice until they come to the ophthalmologist for loss of vision, and accurate figures must, therefore, be impossible to obtain. However, Fletcher[7] in his careful review says of the vision in oxycephaly: "This is occasionally unimpaired, but in the vast majority of cases sight is very defective."

Sight is, as a rule, impaired quite early in life. Meltzer's[8] tabulation of 20 cases illustrates this point:

	Deformity first noticed.	Blindness first noticed.
At birth	13	1
During first year	..	1
During second year	7	1
During third year	..	10
During fourth year	..	3
During fifth year	..	1
During sixth year	..	3

It is particularly worth noting here, too, that diagnosis is possible in the great majority of cases before vision has been lost.

Choice of operation for both preventive and palliative operation depends upon the underlying pathology and, unfortunately, much confusion has arisen from a long-standing difference of opinion as to whether the optic nerve disturbance has its origin in simple constriction by a narrowed optic foramen or in increased intracranial pressure. The first of these theories forms the basis for palliative canal widening operations, which have been performed a number of times. It is founded on 4 necropsies, 1 by Michel[9] (1873), 1 by Ponfick[10] (1886), 1 by Manz[11] (1887) and 1 by Behr[12] (1910). These have been so frequently referred to in support of the theory that we have examined 3 of the original reports for details. Michel's patient, a boy, aged fifteen years, blind since birth, showed optic nerves very narrow and flat, with the sheath filled and apparently distended with a peculiar granulation tissue. There was some evidence of syphilis. The narrowing and flattening of the nerve extended from the chiasm to the optic bulb; the diameter of both nerves within the sheath was the same without and within the foramen, while the horizontal diameter was 0.5 mm. and 0.3 mm. less within the foramen. In this case compression of the nerve obviously had occurred both within the foramen and in the intracranial cavity. The slight additional compression in the foramen may have been, and apparently was, due to an overgrowth of granulation tissue within the optic sheath rather than primarily to narrowness of the canal, about which no exact details are given. Ponfick's report has not been obtainable. Manz's necropsy was done hurriedly, and he states that no direct observation of the foramen was made; he did, however, note that all the foramina observed were widened and that the anatomy of the bones of the skull, especially at the base, was much distorted. Manz based his deduction that the foramen was narrowed on an observed constriction ("Einschnurung") of the nerve at its point of entrance into the foramen.

Behr, in a report to be cited presently, found a similar constriction, but gave it a different explanation. Dorfmann[13] in a dried museum skull found a narrowing of the foramen and, in addition, noted a deep depression of the median portion of the anterior fossa, the cribriform plate deeply depressed, a very deep optic groove and other deformities. Weiss and Brugger,[14] in 4 skulls, Vortisch,[15] in 1, and Enslin,[16] in 6, failed to find narrowing of the optic foramen. Larsen[17] and Bedell[18] in necropsies likewise failed to find it. White,[19] in his recent roentgenologic measurements in patients with optic atrophy, found the optic foramina normal in 2 oxycephalics and definitely enlarged in 4. Both Dorfmann and Behr found the nerve flattened and elongated from the chiasm distally, thus presenting evidence of intracranial pressure or stretching. Behr found a remarkable displacement of the relations between the optic nerve,

foramen and internal carotid artery resulting in pressure on the nerve at the margin of the inner end of the foramen by the artery, which formed part of the internal wall of the foramen. The bony part of the foramen was not narrow. The nerve was flattened and so elongated and displaced that the chiasm rested on the dorsum sellæ.

The evidences of profound dislocation of the normal anatomic relationships at the base in tower skull are many, and cannot all be cited here. The cribriform plate has often been found deeply depressed, and in Larsen's case a hernia of the brain into the nose had occurred. The great wing of the sphenoid has usually been found directed transversely instead of obliquely, thus forming the posterior instead of the lateral wall of the orbit which was accordingly shortened and deformed and its axis changed. The vertical diameter of the orbit may be lessened by as much as 10 mm. (Friedenwald[20]) by downward pressure from above. Dorfmann also noted an accompanying synostosis of the hard palate, causing a high and narrow palatal arch, with marked deviation of the nasal septum. The evidences of increase of intracranial pressure are usually clear and sometimes extreme. The convolutional markings are deep on the calvarium and on the superior walls of the orbit, the former giving a striking roentgenographic picture. The cranial fossæ are often deepened. The clinical symptoms and the appearance of choked disk in several cases seen early,[7, 13] also testify to increased pressure.

In short, it is clear that the interference with skull development from synostosis, especially of the coronal and sagittal sutures, leads to a profound and widespread anatomic dislocation. The skull, unable to expand in all the normal directions, under the growth pressure of the brain is forced to expand at the remaining points of least resistance—the posterior and lateral portions of the calvarium, the cribriform plate, etc. If the compensatory deformities so produced are inadequate there results a progressive rise in the intracranial pressure. This is a gradual process and the pressure apparently does not reach the critical point at which damage to the optic nerve is produced until compensatory expansion has reached its limits. Clinically, this is not often before the third year. In some cases it may be that deformities of the body or wings of the sphenoid lead to narrowing of the optic foramen or to pressure on the nerve by a displaced carotid artery, but even here it seems likely that such changes are traceable to compensatory malformation of the bones of the cranial base from brain pressure. If this be true it forms an added argument for attempting correction before deformity is far advanced. From both views of the pathology, linear craniectomy sufficiently extensive to permit adequate expansion of the growing skull and brain seems to be a logical and justifiable means of prevention of further deformity and of eventual loss of eyesight.

Simple extirpation of the synostosed suture, as suggested by Mehner is probably not enough, and in our opinion a cruciform incision extending nearly the whole length of the coronals and from the bregma to the lambda should be performed unless the sagittal suture is wide open throughout its length. This opinion is based on the fact that when such an excision is made the skull at once expands, spreading the artificial suture and releasing the dura and brain from the tension existing at the time. This phenomenon is not noticeable until the excision has been made in both directions. Another reason is found in the fact that previously open coronal sutures may close prematurely and increase the disability. This occurred in our patient, both of whose coronals were wide open at the age of one month. Between that time and the age of six months, when he was operated upon, the head had rapidly changed from scaphocephalic to brachycephalic, and at operation one of the coronals was found to be closed. It seems clear from the cases reported in the literature and those we have seen that closure of the coronals is by far more serious, in respect to deformity and loss of vision, than that of any of the other sutures.

The operation should be performed as early as possible, before malformation has progressed too far and heightened pressure has begun to develop. The most promising period in our opinion is during the first six months; after the second year satisfactory results are hardly to be expected. As shown in the accompanying graph, growth of the skull and brain is very rapid during early infancy. The normal skull circumference during the first six months attains about 40 per cent of its postnatal growth, and during the first year more than one-half. During the first six months the brain increases in weight about 85 per cent and during the first year 135 per cent.[21] After the first year growth of both skull and brain become progressively slower. The reason for the rapid development of compensatory deformities from synostosis during the first year is obvious, and it is equally obvious that if these and their sequelæ are to be prevented the earlier operation is done the better.

Diagnosis presents few difficulties. Characteristic deformities appear, as a rule, early in infancy and frequently at birth. A ridge along the closed suture can often be felt. The abnormally small head of anencephalic microcephaly is readily distinguished from the head distorted by synostosis, in which the decrease in one dimension is compensated for by increase in another. In the former symptoms of idiocy are early manifest; in the latter mental defects are, as a rule, absent, but if they occur at all they appear much later, usually in late childhood. Symptoms and signs of increased intracranial pressure are wanting in microcephaly. Roentgenograms are usually of value, but in infancy the sagittal is not always easily demonstrable through its whole extent, and a recently closed suture may continue to show as an ill-defined line of lessened density.

Conclusion. In conclusion, it should be said that while synostotic deformities are not very uncommon, they seldom constitute a presenting complaint. Parents, as a rule, do not seek medical advice for a peculiarity of appearance, best unremarked, in their children. If the diagnosis is to be made more often and earlier it devolves upon the physician, particularly the pediatrician and the obstetrician, in the routine of private or clinic practice, to focus his attention for a moment on the skull configuration of each infant and child he sees. Discovering one of these cases, he should realize that the chances of eventual blindness are extremely high, and that operative interference for restitution of normal skull development and for the conservation of vision may be undertaken with small risk.

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GENERAL PARESIS.

A Clinico-pathologic Study with Especial Reference to the Significance of the So-called "Typical" Laboratory Findings.

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Among the various forms of mental disease there is none which may start in such a variety of ways and exhibit such a protean symptomatology as general paresis. It has been known for a long time that the initial symptoms of paresis are often similar to those of the psychoneuroses; the onset may also be with excitement, depression, or a paranoid trend. Recently Bunker[1] has reviewed the records of 74 paretics, interviewed their relatives, and found that some of them showed psychic abnormalities for at least four years before the mental breakdown occurred. Irritability, "nervousness," bradyphrenia and other common neuropsychiatric complaints were among some of the frequent early symptoms in Bunker's cases. How often is the significance of such symptoms overlooked!

It goes without saying, therefore, that long before the old conception of paresis, namely, delusions of grandeur and dementia, occurs, that there must be prodromal symptoms which may antedate the acute mental upset by years.

Paresis is such a common mental disease (making up, as it does, 20 per cent of those in mental hospitals) and may masquerade under such different guises that it should always be thought of in any psychiatric disturbance occurring between the ages of twenty-five and seventy years; furthermore, juvenile paresis is common enough in the psychoses of childhood.

From a diagnostic standpoint too much stress has been laid upon the grandiose form of paresis and too little upon the other and more common ways in which the disease asserts itself. Once general paralysis is in full bloom with changes in character, delusions of grandeur, physical signs and mental deterioration a tyro can, or at least should, make the diagnosis with facility. If we have in the form of laboratory examinations anything which will anticipate the almost irreparable brain damages which occur in paresis it would be a means of saving at least a few cases from mental catastrophies.

From the pathologic angle our conception of paresis is a syphilitic meningoencephalitis characterized by a fibrous thickening and infiltration of the meninges with round cells of the lymphocytic and plasma type, the infiltration being particularly limited to the deeper pial layers. In the cortex the findings are a breaking up of the architecture independent of the vascular supply, perivascular infiltration with cells identical with those of the pia, the occurrence of rod cells in great number, and new vessel formation. By means of the newer staining methods we can detect the increase of iron and enormous numbers of so-called Hortega and Cajal cells of the glial type. A certain percentage of cases, probably not over 15, have sclerosis of the posterior columns of the cord and the usual syphilitic meningitis, producing the clinical picture that is commonly called taboparesis. Remissions, either spontaneous or as a result of therapeutic measures, may bring about decided improvement in the pathologic picture.

Since Lange described the gold-sol reaction in 1912 a considerable literature has sprung up on the subject, and it has come to be an integral part of every complete spinal-fluid examination. The so-called paretic curve in itself does not mean paresis but may occur in a number of other conditions such as multiple sclerosis, neurosyphilis other than paresis, meningitis especially tuberculous, occasionally in cerebral tumors and at times in other conditions such as epidemic encephalitis; certainly a syphilitic curve frequently is found in the foregoing diseases. While the paretic curve is not pathognomonic of general paresis, the absence of it in the spinal fluid of a paretic, virgin from the therapeutic standpoint, is a rather rare occurrence. When the paretic curve is combined with other cerebrospinal fluid evidences of syphilis it is of great diagnostic importance. We refer of course to a positive Wassermann reaction with different amounts of the fluid, pleocytosis and an increase of globulin. If all the laboratory tests enumerated are positive and in addition a positive Wassermann reaction in the blood is found, are we justified in assuming that such a case is incipient general paralysis of the insane even in the absence of mental symptoms? If mental symptoms are present, is such a case always paresis or may the patient have neurosyphilis and a psychosis nonparetic in origin?

To answer these questions, at least in part, we have analyzed the records of cases which were correctly or incorrectly diagnosed general paresis, who died and whose brains were obtained and examined. In addition we reviewed the histories of 10 cases in which the diagnosis of paresis was made or was considered because of the laboratory tests, and later we examined the brains of the series.

We have divided the cases into the following groups:

1. Thirty-nine cases in which the diagnosis of paresis was made on the history, physical and mental examinations and laboratory

tests and the diagnoses were proved to be correct by microscopic studies.

2. Six cases with the so-called typical laboratory findings; the cases were proved by examination of the brains to be paresis but were diagnosed incorrectly.

3. Twelve cases diagnosed paresis, some of whom had paretic laboratory findings but on microscopic examination were found not to have general paralysis of the insane.

4. Ten cases in which the diagnosis of paresis was considered and in which the laboratory findings were suggestive but the cases were neither diagnosed paresis nor did they have paresis on microscopic study.

Group 1. Of the patients who fell under this heading, every one to a greater or less degree had laboratory findings indicative of paresis. However, as in any group of cases the clinical records of which are studied after death, many examinations were missing but the information available is well worth while summarizing. Of the 39 cases all but 3 had positive Wassermann reactions of the blood, giving a percentage of 92. Of the 3 cases who had negative blood Wassermanns one had received a great deal of intravenous therapy. The spinal fluid Wassermann was not done in 1 case; in a second the fluid was anticomplementary; in all but 1 of the remainder it was 4+. The 1 case which showed a negative spinal fluid Wassermann was admitted to the Philadelphia General Hospital in coma, had status epilepticus and died in a few hours. Subsequent investigation of the woman's history showed that she had received intravenous therapy over a prolonged period. The colloidal-gold curve was paretic in type in every case except 1; this patient had had antisyphilitic treatment and the gold test in this case showed the syphilitic curve on two occasions, and one time gave no curve at all. The cerebral pathology, however, was typical of paresis. The cells in the spinal fluid were estimated in all but 4 cases and the average was 31, the count ranging from 1 to 400. The globulin was not estimated in 8 cases, in the remainder it was negative in 1 and increased in the others.

Group 2. While this series of cases is not large, a consideration of them is of great importance. It proves conclusively, at least to us, that mental symptoms when combined with the so-called typical laboratory findings of general paresis always make that diagnosis the most likely one and that the burden of proof is on the shoulders of him who says such a case is not one of general paresis. In fact he who persistently and stubbornly refuses to acknowledge the importance of such a combination is either a super-diagnostician or one whose audacity will constantly get him into trouble.

Group 3. This division consists of 12 cases which were diagnosed general paresis. Some of them had the laboratory findings extremely

suggestive of such a condition but pathologically none of them were general paralysis of the insane.

TABLE I. GROUP 2.—CASES OF PARESIS DIAGNOSED INCORRECTLY.

Clinical diagnosis.	Laboratory findings.						Pathologic diagnosis.
	Blood Wassermann.	Spinal Wassermann, cholesterin.	Spinal Wassermann, Noguchi.	Cells per cu. mm.	Globulin.	Colloidal-gold curve.	
Right cerebral hemorrhage and tabes . .	Not done	4+	4+	3	Not done	5555543511	Tabo-paresis
Amebic abscess of liver and tabes	Neg.	2+	Neg.	22	Trace	5555554310	Tabo-paresis
Syphilitic meningitis . .	4+	4+	4+	5	2+	5555555520	Paresis
Tabes	4+	4+	4+	0	Trace	5555432100	Paresis
Syphilitic meningomyelitis . .	4+	3+	3+	60	4+	5555543211	Paresis
Dementia præcox . .	4+	4+	4+	6	Neg.	5555543100	Paresis

Group 4. This group covers 10 cases in which the diagnosis of paresis was considered and in which the laboratory findings were suggestive but the cases were neither diagnosed paresis nor did they have paresis on microscopic study.

Comment. An analysis of the records which we have presented shows that the vast majority of cases of general paresis have strongly positive evidences of syphilis in the blood and spinal fluid, including the presence of the paretic gold curve. Cases of neurosyphilis other than general paresis, however, may show almost identical laboratory reactions. Sicard and Haguenau[2] believe that the favorable results in the treatment of general paresis reported by American and Austrian writers are due to the inclusion in their series of certain cases of cerebral syphilis. Our series of cases certainly bear out this fact. If one, in making the diagnosis of general paralysis of the insane, depends entirely upon the so-called paretic laboratory findings he will often be led astray; an incorrect belief in the infallacy of these tests, as a short cut to diagnosis, may be engendered by a feeling of uncertainty in one's diagnostic ability in the specialty of neuropsychiatry.

TABLE II. GROUP 3.—CASES DIAGNOSED PARESIS INCORRECTLY.

Sex.	Age.	Clinical summary.	Laboratory findings.						Pathologic diagnosis.
			Blood Wassermann.	Spinal Wassermann, cholesterin.	Spinal Wassermann, Noguchi.	Cells per cu. mm.	Globulin.	Colloidal-gold curve.	
F. . . .	57	Incontinence, dizziness, generalized twitchings; pupils fixed; perforated septum; reflexes increased, Jacksonian convulsions; euphoria; delusions of grandeur	4+	4+	4+	4	None	3555554221 4444442211	Gumma left frontal lobe; softening, right frontal lobe; gumma, left parietal region
M. . .	61	Attacks of temporary paralyses of lower extremities; incontinence of feces; alcoholic; pupils sluggish; reflexes increased; euphoric; grandiose	Neg.	Neg.	Neg.	2	Faint trace	0012211000	Arteriosclerosis with areas of softening
F. . . .	60	Sick two years, weakness of hands; low mentality; Jesus spoke to her; pupils rigid; loss of speech; coma	4+	4+	4+	20	Trace	1123321000	Arteriosclerosis Thrombosis of superior longitudinal sinus
M. . .	55	Right hemiplegia and aphasia	4+	4+	4+	80	Trace	5555543100	Thrombosis with softening
M. . .	56	Five weeks ago dizziness, headache, paresthesia on left side; recovered in two weeks; later paralyzed on left side; pupils sluggish; aortic disease; speech thick; mental deterioration	4+	4+	4+	240 156	Not done	5544321100	Arteriosclerosis; meningeal syphilis; softening of left basis pontis and left lobe of cerebellum

F. . . .	58	Ill five months, headaches, dysarthria, girdle sensation, difficulty in walking; right hemiplegia and aphasia	4+	4+	4+	383	Faint trace	5555555432	Multiple areas of thrombotic softening due to meningovascular syphilis
F. . . .	40	Carbuncle followed by erysipelas, then period of excitement and confusion; stupor; neck rigid; no Kernig; reflexes decreased; right pupil fixed; left sluggish	4+	Neg.	Neg.	0	Neg.	0001100000	Glioma of brain
F. . . .	?	Sick two years; "cold and aches;" past week confused; pupils unequal and fixed; generalized spasticity, catatonic, depressed, hallucinations, disoriented	4+	Neg.	Neg.	0	Neg.	1223331000	Pellagra
M. . .	37	Coma, convulsions, paralysis right lower extremity, euphoria, delusions of marital infidelity, auditory hallucinations; alcoholic	4+	4+	4+	30 240	Pos.	1123340000 1123343310	Cerebral syphilis; meningovascular type
M. . .	56	Epileptic fits for fifteen years; admitted in coma; left pupil rigid; reflexes increased. Bilateral Babinski	Neg.	Neg.	Neg.	0	Neg.	2234322000	Arteriosclerosis of small vessels
M. . .	60	Numbness in feet, dysarthria, boisterous, profane, threatened to kill wife; spent money foolishly; euphoric, poor memory	Neg.	Neg.	Neg.	8	Trace	0001210000	Arteriosclerosis; multiple areas of softening many small hemorrhages
F. . . .	56	Difficulty in walking; incontinence of urine; stone deaf; pupils small and rigid; no mental symptoms; reflexes increased; bilateral clonus and Babinski	4+	4+	4+	5	Trace	5555555430	Cervical hypertrophic pachymeningitis

TABLE III. GROUP 4.—CASES WITH LABORATORY TESTS SUGGESTING PARESIS BUT NECROPSY FAILING TO VERIFY THAT DIAGNOSIS.

Sex.	Age.	Clinical summary.	Laboratory findings.						Pathologic diagnosis.
			Blood Wassermann.	Spinal Wassermann, cholesterin.	Spinal Wassermann, Noguchi.	Cells per cu. mm.	Globulin.	Colloidal-gold curve.	
F. . . .	60	Pain in stomach for two years; confused, left hemiplegia	Neg.	4+	4+	20	Cloud	2555555544	Syphilitic meningitis
F. . . .	35	Two months prior to death became stuporous, had convulsions of right face	4+	4+	4+	4	Trace	5555554310	Gummatous meningoencephalitis
F. . . .	53	Right hemiplegia one month prior to admission; aphasic, involuntary emotionalism	4+	4+	Not done	8	Trace	5555554310	Cerebral syphilis
M. . .	48	Stroke at twenty-five, second stroke day of admission; depressed, refused to eat, self-accusatory, incontinent; pupils normal; right hemiplegia	4+	4+	4+	55	Trace	5555543110	Cerebral meningovascular syphilis; aneurysm of basilar artery

F. . . .	33	Ill for one month, drowsy, irritable, depressed; auditory, visual and olfactory hallucinations, violent tremors, pupils unequal, sluggish	4+	4+	Not done	95	Not done	5555443100	Softening, left pallidum and right thalamus; meningovascular syphilis
M. . .	24	Stroke one year prior to admission; second stroke six months later; bedridden, dysarthria, dysphagia, exaggerated deep reflexes	4+	4+	4+	6	Trace	5555554221	Gummatous meningitis and gumma of pons
M. . .	74	For two months burning in left leg; pupils unequal, irregular, sluggish reaction; gummata of leg; six weeks after admission became stuporous and died	Neg.	Neg.	Neg.	Not done	Not done	5554321000	Left subdural hemorrhage; arteriosclerosis
M. . .	32	Unconscious with generalized convulsions on admission; fits for eight months previously; pupils irregular and sluggish; left patellar reflex absent	4+	Neg.	Neg.	20	Cloud	4445443100	Meningovascular syphilis and gumma left parieto-occipital region
M. . .	42	History and physical signs of tabes, but with bilateral Babinski	Neg.	4+	Not done	40	Trace	2444432110	Diffuse neurosyphilis
M. . .	23	Emaciated, prostrated, soon became comatose; cough and expectoration	4+	Neg.	Neg.	5	Trace	5555542200	Syphilitic endarteritis

While the diagnostician by his too blind adherence to the importance of laboratory examinations may frequently confuse cerebral syphilis with general paresis, it is much more certain that he who diagnoses general paresis without laboratory backing is in greater danger of error. In the cases of Group 3 diagnosed general paresis without strong confirmation by the laboratory, the diagnosis was invariably wrong, although in some of the cases the laboratory in part supported the diagnosis. This is especially so as far as the gold test was concerned. It has frequently been observed that alterations in the colloidal-gold curve are common in many organic affections of the central nervous system. The presence of a paretic or syphilitic curve in the fluid without other evidence of syphilis points rather away than toward the diagnosis of neurosyphilis and particularly paresis.

Another phase of the subject which is of great importance is the correlation of mental symptoms such as depression, irritability, nervousness, excitement, delusions and dementia, with strongly positive evidences of syphilis in the blood and the entire line of syphilitic reactions in the spinal fluid. Some of the cases which we report had positive laboratory tests for syphilis, had definite mental symptoms and yet were not general paresis; but the number of these cases was small. Some of them, however, would defy the most expert clinician in his attempt at differential diagnosis; thus one of our cases in Group 3 had gummas in the left frontal and left parietal regions and softening of the right frontal lobe, paretic findings in the blood and spinal fluid, euphoria, delusions of grandeur, fixed pupils, and hyperreflexia. Who would be so bold as to say that such a case was not general paralysis of the insane? Or consider one of the cases in Group 4: a female, aged 33 years, ill for one month; she was drowsy, irritable, depressed and violent; she had tremors of the face, tongue and hands, the pupils were unequal and sluggish; in addition the patient had auditory, visual and olfactory hallucinations and while there was no history of alcoholism it is not unlikely that she indulged. The laboratory tests pointed strongly to general paresis as the diagnosis. She had softening of the left pallidum and right thalamus and diffuse meningovascular syphilis. Are there many who would have thought that the hallucinations in this case ruled out paresis? We doubt it.

A number of cases with clinical evidence of gross organic disease of the brain or cord and laboratory tests suggestive of paresis proved almost invariably to be cerebral syphilis or other forms of neurosyphilis rather than paresis. While an occasional case showing both mental symptoms and the so-called paretic, laboratory results may be found to be nonparetic; this is certainly not the rule, but it does occur.

Conclusions. Review of the records and the necropsy results in the 67 cases which we report leads us to the following conclusions:

1. An untreated case of general paresis will show blood and spinal fluid evidences of syphilis. These tests will usually be markedly positive, including pleocytosis, an increased amount of globulin and the paretic gold curve.

2. An untreated case diagnosed general paresis without strong confirmatory laboratory backing is practically always something else.

3. A certain limited number of cases showing mental symptoms and evidence in the blood and spinal fluid of a paretic nature may, on microscopic studies of the brains, be proven not to be instances of general paresis.

4. A brain which shows a gross organic condition such as hemorrhage, thrombosis or gumma rarely shows microscopic evidences of general paresis.

5. Strong laboratory evidences of syphilis such as mentioned above without mental symptoms are not enough to allow the diagnosis of incipient general paresis.

REFERENCES.

1. Bunker: Am. Jour. Med. Sci., 1926, **171**, 386.
2. Sicard and Haguenau: Bull. Soc. méd. d. hôp. d. Paris., 1924, **48**, 1517 (abstr. J. Am. Med. Assn., 1924, **83**, 2120).

REVIEWS.

CLINICAL APPLICATIONS OF SUNLIGHT AND ARTIFICIAL RADIATION. By EDGAR MAYER, M.D., of Saranac Lake, N. Y. Pp. 550; 69 illustrations. Baltimore: The Williams & Wilkins Co., 1926. Price, $10.00.

THIS book is a most timely one, particularly in view of the efforts being made at this time to standardize this type of work. It contains twenty-six chapters, dealing with the historical, experimental and physiologic action of ultraviolet radiation on animal and plant life. The bibliography is most extensive, representing what one would regard as a lifetime of investigation. The author has presented his research in very good form, and anyone doing this type of work would do well to have the book, which is really an encyclopedia containing all of the experimental work pertaining to this field, with its clinical application in the treatment of disease. The publishers are to be commended upon the paper and print and also the unique way in which they include the various members of their staff, giving credit where credit is due. E. P.

A MANUAL OF PHARMACOLOGY AND ITS APPLICATIONS TO THERAPEUTICS AND TOXICOLOGY. By TORALD SOLLMANN, M.D., Professor of Pharmacology and Materia Medica in the School of Medicine of Western Reserve University, Cleveland. Third edition, entirely reset. Pp. 1184. Philadelphia: W. B. Saunders Company, 1926. Price, $7.50.

THE rapid advances of pharmacologic investigation are well illustrated in the addition of 120 pages and 1200 bibliographic titles to this edition, in spite of most careful pruning. Numerous new drugs are included, headed by insulin, and various new concepts, together with the tenth edition of the Pharmacopœia, have necessitated rewriting the larger part of the important matter. The book remains of equal value with the previous editions. (See AM. J. MED. SCI., 1923, **165**, 285.)

E. K.

PRINCIPLES OF MEDICAL TREATMENT. By GEORGE C. SHATTUCK, M.D., A.M., Assistant Professor of Tropical Medicine, Harvard Medical School. Sixth edition, revised and enlarged. Pp. 256. Cambridge: Harvard University Press, 1926.

THE sixth edition of this work continues its former usefulness. It is a very handy pocket size book and contains a very complete and satisfactory outline of medical treatment. It seems a little overcautious to omit the dose of quinidin sulphate at this late date. Anyone justified in using this book should be trusted properly to employ such a drug.

O. P.

A SOUND ECONOMIC BASIS FOR SCHOOLS OF NURSING AND OTHER ADDRESSES. By MARY A. NUTTING, R.N., M.A., Professor Emeritus, School of Health, Teachers' College, Columbia University. Pp. 372. New York: G. P. Putnam's Sons, 1926.

THE author has been an outstanding leader in nursing education for many years. The present volume puts into permanent form an extreme valuable collection of addresses bearing on the growth and development of schools of nursing. These papers present the findings of the author's own experience in the education of nurses, as superintendent of Johns Hopkins School of Nursing and later as the director of the Department of Nursing and Health at Teachers' College, Columbia University. They are stimulating, outspoken discussions of the dominant problems of nursing education, the root of which is largely found to be economic in nature.

S. G.

PHYSIOLOGY AND BIOCHEMISTRY IN MODERN MEDICINE. By J. J. R. MACLEOD, M.B., LL.D. (ABERD.), D.SC. (TOR.), F.R.S., Professor of Physiology in the University of Toronto, Can. Fifth edition. Pp. 1054; 291 illustrations. St. Louis: C. V. Mosby Company, 1926. Price, $11.00.

A NEW edition of the author's textbook—considered by many the best on its subject in English or any other language—is an important event in medical education, and four years is a long time between editions in this rapidly expanding subject. This edition has been made even more valuable to medical students by the addition of a section on the physiology of the special senses by J. M. D. Olmsted and Redfield's section on the neuromuscular system has been expanded to include the extensive field of nerve muscle physiology. One's curiosity is aroused by the position of the neuromuscular system and the special senses between the blood and lymph and the

circulation of the blood. The various additions necessitated the addition of 50 pages and 48 illustrations, without, however, adding appreciably to the unwieldiness of the book. E. K.

PRINCIPLES AND PRACTICE OF CHEMOTHERAPY, WITH SPECIAL REFERENCE TO THE SPECIFIC AND GENERAL TREATMENT OF SYPHILIS. By JOHN A. KOLMER, M.D., DR.PH., D.SC. (HON.), Professor of Pathology and Bacteriology in the Graduate School of Medicine of the University of Pennsylvania and Member of the Research Institute for Cutaneous Medicine. Pp. 1106; 82 illustrations. Philadelphia: W. B. Saunders Company, 1926. Price, $12.00.

IN this monograph the author has largely fulfilled his expressed intention of covering the field of modern chemotherapy in all its medical and surgical aspects. The discussion includes sections on general principles, the chemotherapy of bacterial and mycotic diseases, trypanosomal diseases, spirochetal diseases other than syphilis, protozoan and metazoan diseases, and the chemotherapy of anemias, malignant tumors and other conditions of uncertain etiology. Of the 1054 pages, 607 are devoted to the chemotherapy of syphilis, the discussion broadening into the fields of serologic diagnosis, immunologic and pathologic background, technical detail and valuable summaries of the modern refinements of biologic testing and evaluation of antisyphilitic medicaments.

The appraisal of so genuinely monumental a work by a single reviewer must be a matter of great difficulty. One's first impression relates to the author's generally successful effort to illumine an encyclopedic knowledge of laboratory procedure, usually inaccessible or incomprehensible to the clinician, with a by no means narrow clinical experience. That the laboratory furnishes the stronger leg is evident, but the gait and effectiveness of the work for the clinician is not seriously impeded thereby. It is no mean accomplishment to produce a single volume in whose pages can be found a formula for a soothing antiseptic paste for wounds, every known method for the administration of quinin, the germanium therapy of pernicious anemia (even though of doubtful value), a usable technique for getting blood from babies and the malaria inoculation treatment of paresis. As in very work which seeks to harmonize medical knowledge under an artificial or man-made rather than a biologic keynote, one observes occasional strange propinquities.

The author's huge industry, his fairness and completeness of statement, even of opposing views, his excellent critical judgment and scholarly particularity are apparent in every chapter. The

work done in placing the literature of syphilotherapy at the disposal of the clinician would alone justify the book. The development is logical and cohesive, and the discussion of first principles on syphilis forms a particularly sound background for the sadly needed rationalization of modern treatment. If there is any adverse criticism necessary on this point, it is one of insufficient detail on known treatment results in certain phases of the disease.

On many aspects of syphilis the author is qualified to speak *ex cathedra* as an expert of international reputation, and from his comments specialists will glean many points of interest and challenge. His endorsement of arsphenamin (606) as the premier arsenical comes as a breath of relief in a "neo"-saturated world. His evaluation of bismuth, while too brief for enthusiasts, displays a refreshing sanity that the reviewer believes time will fully justify. Mercury is not dead yet! The statements on the clinical relations of the Kolmer Wassermann test will be listened to with respect by every clinician who knows the worth of the author's contributions in this field. The detail of laboratory testing procedure is invaluable, the technical methods in clinical practice adequate and well illustrated, though one cannot but regret the inclusion of the sitting lumbar puncture and the syringe injection of medicaments into the spinal canal.

The book, very properly, is a personal one, but justifiably so, and is kept in excellent balance by the full presentation of the literature. One cannot but wish at times that the bases of the author's own clinical "credos" could have had fuller discussion and a little space for it might have been saved by devices of literary condensation, including a less frequent use of the rhetoric question. The format of the work, perhaps inevitably, because of the volume of material, buries some jewels for the practitioner in the sand of type, and presents at times an unbroken uniformity of face which fatigues the eye. The proofreading is poor, even for so large a book, and will irritate the meticulous.

These detractions are essentially minor. The work will meet the assured and deserved success of a masterly "Arbeit," which accomplishes that only too rare feat in medical literature, of giving rationalizing perspective and usable detail between one pair of boards. J. S.

ELECTROTHERMIC METHODS IN NEOPLASTIC DISEASES. By J. DOUGLAS MORGAN, B.A., M.D., Instructor in Radiology, University of Pennsylvania Graduate School of Medicine, Philadelphia. Pp. 172; 36 illustrations. Philadelphia: F. A. Davis Company, 1926. Price, $2.50.

THIS small book is a very timely and concise presentation of the subjects of electrodesiccation and electrocoagulation and satisfies a

need that has long been wished for. It contains nine chapters dealing with the following subjects: Electricity, First Principles and Definitions; Chemical and Physical Effects of Currents; Surgical Diathermy, Its History, Terminology and Uses; Apparatus; Electrodesiccation; Electrocoagulation; General Summary; Tissue Cutting by Means of the High-frequency Current; Practical Exercises in the Use of the Currents. The subjects are well presented and the book is recommended to all who are interested in this particular field. E. P.

THE PRINCIPLES OF ANATOMIC ILLUSTRATION BEFORE VESALIUS: AN INQUIRY INTO THE RATIONALE OF ARTISTIC ANATOMY. By FIELDING H. GARRISON, M.D. Pp. 58; 26 illustrations. New York City: Paul B. Hoeber, Inc., 1926. Price, $2.50.

A CHARMING work, full of the author's well-known and unapproachable erudition, in which he shows that the medical man may learn a good deal from the artist. Much physiology, pathology and ethnology, he points out, is exhibited in the paintings and sculptures by paleolithic and neolithic man. The Renaissance artists who made such conscientious dissections seemed, without a direct study of medicine, to understand the physiology of muscular motion and of expression. None was greater in this respect than Leonardo da Vinci.

Both in the entertaining preface and throughout the text the author points out the fact that the true physician must have the artist's vision—the artist's eye to see. The return to the practice of "seeing" and to the independent thinking that goes with it is, in Garrison's opinion, the greatest desideratum of our time. D. R.

BRAINS OF RATS AND MEN: A SURVEY OF THE ORIGIN AND BIOLOGICAL SIGNIFICANCE OF THE CEREBRAL CORTEX. By C. JUDSON HERRICK, Professor of Neurology, the University of Chicago. Pp. 382; 50 illustrations. Chicago: The University of Chicago Press, 1926.

A VERY readible book based on the lectures given in 1924 at the University of California on "Mechanisms of Control of Animal Behavior." It takes up particularly "the two species of mammals whose behavior has been more intensively studied under conditions of laboratory control than any others—rats and men." The evolution of the cerebral cortex from fish to man is considered particularly as regards function. Not only should this book appeal to the Neurologist and Psychiatrist, but to all who are interested in man and his problems. N. W.

BOOKS RECEIVED.

Tuberculosis: Bacteriology, Pathology and Laboratory Diagnosis. By EDWARD R. BALDWIN, M.D., S. A. PETROFF, PH.D., and LEROY U. GARDNER, M.D. Pp. 342; 82 illustrations. Philadelphia: Lea & Febiger, 1927. Price, $4.50. (To be reviewed later.)

Nursing Mental and Nervous Diseases. By ALBERT COULSON BUCKLEY, M.D. Pp. 312; 57 illustrations. Philadelphia: J. B. Lippincott Company, 1927. Price, $3.00. (To be reviewed later.)

The Treatment of Chronic Arthritis and Rheumatism. By H. WARREN CROWE, D.M., B.CH. (OXON.), M.R.C.S. Pp. 196; 18 illustrations. New York: Oxford University Press, American Branch, 1927. (To be reviewed later.)

Solubles ou Insolubles. By HENRI DROUIN. Pp. 96; 10 illustrations. Paris: Paul Martial, 1927.

Basal Metabolism in Health and Disease. By EUGENE F. DU BOIS, M.D. Second edition. Pp. 431; 92 illustrations. Philadelphia: Lea & Febiger, 1927. Price, $5.00. (To be reviewed later.)

Elementary Bacteriology and Protozoölogy for the Use of Nurses. By HERBERT FOX, M.D. Fourth edition. Pp. 242; 74 illustrations. Philadelphia: Lea & Febiger, 1927. Price, $2.50. (To be reviewed later.)

Outlines of Common Skin Diseases. By T. CASPAR GILCHRIST, M.D. Pp. 54; 5 illustrations. Baltimore: Williams & Wilkins Company, 1927. Price, $1.50. (To be reviewed later.)

The Diseases of Infants and Children. By J. P. CROZER GRIFFITH, M.D., PH.D., and A. GRAEME MITCHELL, M.D. Two volumes. Second edition. Pp. 1715; 461 illustrations. Philadelphia: W. B. Saunders Company, 1927. Price, $20.00 for two volumes. (To be reviewed later.)

Clinical Methods. By ROBERT HUTCHISON, M.D., F.R.C.P., and HARRY RAINY, M.D., F.R.C.P. (EDIN.), F.R.S.E. Pp. 688; 167 illustrations. New York: Paul B. Hoeber, Inc., 1927. Price, $5.00. (To be reviewed later.)

A Terminology of Disease. By ADRIAN V. S. LAMBERT, M.D. Third edition. Pp. 158. New York: Paul B. Hoeber, Inc., 1927. Price, $2.25. (To be reviewed later.)

Index and Handbook of X-ray Therapy. By DR. ROBERT LENK. Translated by T. I. CANDY, M.B., B.CH. Pp. 121. New York: Oxford University Press, American Branch, 1927. Price, $2.25. (To be reviewed later.)

Methods and Problems of Medical Education (Sixth Series). Pp. 275; illustrated. New York: Division of Medical Education, Rockefeller Foundation, 61 Broadway, New York City, 1927. Continuation of a series useful to medical pedagogues.

Physicians of the Mayo Clinic and Mayo Foundation. Pp. 578; 611 illustrations. Philadelphia: W. B. Saunders Company, 1927. Price, $7.00. Contemporary biographies of the Mayo Staff.

Diseases of the Heart. By FREDERICK W. PRICE, M.D., F.R.S. (EDIN.). Pp. 534; 249 illustrations. New York: Oxford University Press, American Branch, 1927. (To be reviewed later.)

Heliotherapy. By A. ROLLIER, M.D. Translated by G. DE SWIETOCHOWSKI, M.D. Pp. 318; 273 illustrations. New York: Oxford University Press, American Branch, 1927. (To be reviewed later.)

A Manual of Materia Medica for Medical Students. By E. QUIN THORNTON, M.D. Second edition. Pp. 384. Philadelphia: Lea & Febiger, 1927. Price, $4.50. (To be reviewed later.)

Surgical Applied Anatomy. By SIR FREDERICK TREVES, BART. Reviews by C. C. CHOYCE, C.M.G., C.B.E., M.D. Eighth edition. Pp. 727; 162 illustrations. Philadelphia: Lea & Febiger, 1927. (To be reviewed later.)

The Enlarged Prostate. By KENNETH M. WALKER, M.A., M.B., B.C. Pp. 193; 59 illustrations. New York: Oxford University Press, American Branch, 1927. (To be reviewed later.)

Symbionticism and the Origin of Species. By IVAN E. WALLIN, SC.D. Pp. 171; 2 illustrations. Baltimore: Williams & Wilkins Company, 1927. Price, $3.00.

Manual of Operative Surgery. By SIR HOLBURT J. WARING, M.D., M.B., B.SC. (LOND.). Sixth edition. Pp. 868; 618 illustrations. New York: Oxford University Press, American Branch, 1927. (To be reviewed later.)

A Textbook of Clinical Neurology. By ISRAEL S. WECHSLER, M.D. Pp. 725; 127 illustrations. Philadelphia: W. B. Saunders Company, 1927. Price, $7.00. (To be reviewed later.)

Manual of Medicine. By A. S. WOODWARK, C.M.B., C.B.E., M.D., F.R.C.P. Third edition. Pp. 523. New York: Oxford University Press, American Branch, 1927. (To be reviewed later.)

Applied Physiology. By SAMSON WRIGHT, M.D., M.R.C.P. Pp. 418; 37 illustrations. New York: Oxford University Press, American Branch. (To be reviewed later.)

Lehrbuch der Geburtshilfe. By PROF. DR. WILHELM ZANGEMEISTER. Pp. 834; 329 illustrations. Leipzig: S. Hirzel, 1927. (To be reviewed later.)

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

JOHN H. MUSSER, M.D.,

PROFESSOR OF MEDICINE, TULANE UNIVERSITY OF LOUISIANA, NEW ORLEANS.

Diabetes: A Statistical Study of One Thousand Cases.—A statistical study of the patients that have been seen in the last four years by JOHN (*Arch. Int. Med.*, 1927, **39**, 67) brings out some interesting data which in part are a confirmation of the statistics obtained by others, but which vary somewhat in some particulars. The statistics include the age and sex, influence of heredity, relation of blood sugar content to glycosuria, the effects of treatment with insulin, the incidence of syphilis in the diabetic, the incidence of operations on diabetic patients and the death rate. Of particular interest are the tables showing the lasting effects of insulin in the treatment of diabetes. It is true that many of these patients have only had insulin for a short time, but it is surprising to find the large number in whom it was possible to discontinue insulin. Another interesting table is the table illustrative of the relation of blood sugar before and at the time of the reaction to insulin. The author shows by his figures that the insulin reaction is not necessarily dependent upon hypoglycemia. In 50 per cent of the cases this was not the cause. In fact, actual hyperglycemia was demonstrated. The author also shows that there is a marked irregularity in the factors that are supposed to play a part in the production of this reaction, as judged by the time relation of the insulin reaction to the dosage of the preparation.

The Mechanism of Pain in Gastric and in Duodenal Ulcer.—The third paper by PALMER (*Arch. Int. Med.*, 1927, **39**, 109), in the study of pain in gastric ulcer, deals with the rôle of peristalsis and spasm. It will be recalled that in 1917 Carlson, employing the so-called balloon method showed that intermittent ulcer pain occurred with gastric peristalsis, and he concluded that the pain in this condition was due

to muscle tension. The author investigates Carlson's results and elaborates upon his methods. In addition to the patient swallowing a rubber balloon, he also has him swallow duodenal tubes. Kymographic studies that he has made with this technique are very well done and illustrate very beautifully indeed the reason for his conclusions. He finds that the pain-producing mechanism is intimately associated with ulcer, but it is not dependent upon gastric motility nor upon pylorospasm. At times gastric peristalsis may cause stimulation to the pain-producing mechanism, but probably more important than peristalsis is the direct sensitizing effect of hydrochloric acid, as shown by producing pain when injected into the stomach previously free of gastric contents and when it is withdrawn through the duodenal tube relieving pain.

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

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Dislocation of the Semilunar Bone.—McBride (*Arch. Surg.*, 1927, **14**, 584) says that reduction of simple dislocation of the semilunar can usually be accomplished by manipulation within the first three or four days and complete return of function can be expected. In cases in which removal of bone is done within two or three weeks, or in which there is mild neurospastic fixation, good function will result, but at least some permanent weakness will remain. Open reduction under the same circumstances promises as good a return of function as removal. There is, however, danger of traumatic arthritis. Untreated patients have from 25 to 75 per cent permanent disability. Open reduction after several weeks or in cases in which neurospastic fixation is severe, should not be attempted, even though in many instances it can be accomplished, for removal is better. Removal in late cases with severe fixation and degenerative changes usually will relieve the pain to a considerable degree, while improvement in function is slight. When fractures of the scaphoid complicate dislocation of the semilunar bone, severe traumatic arthritis is so likely to occur in these cases that closed or open reduction is dangerous. If not accomplished within a few hours after injury, excision is therefore indicated. Removal of the semilunar and whole scaphoid bone seems to give as good results as those secured in cases in which the proximal fragment only is removed and is the method of choice.

Ranula.—Fitzwilliams (*Brit. J. Surg.*, 1927, **14**, 472) states that ranula is a loose term which has been applied to all cystic swellings of

the floor of the mouth whatever their form or origin. These tumors form first in the mouth and then spread, extend or burrow into other regions. Many are in connection with the submaxillary gland, others are not so obviously in connection with this gland and others again have no connection with it. When traced to the region of the sublingual gland, we have no means of telling whether they are mucous or salivary in origin. It is impossible to test the efficiency of the sublingual ducts. The author has no knowledge of anyone passing bristles into the ducts. Moreover there is no exact knowledge of the number of ducts present in each gland. After full logical deductions the author proves that ranula may arise in the salivary glands, including Blandin's gland, and in the mucous glands and nowhere else. There is nothing to favor the view that Fleischmann's bursa exists and there is nothing to connect a ranula with the supposed survival of a cervical sinus.

Causation of the Increased Intracranial Pressure Associated with Tumors within the Cranium.—STOPFORD (*Brit. Med. J.*, 1926, **2**, 1207) says that it is shown that the great vein of Galen is situated in such a position that it may be compressed against the splenium of the corpus callosum indirectly or directly by tumors occupying sites which are known to give rise most constantly to increased intracranial pressure. Such compression is not likely in the case of tumors occupying situations which are known to cause less frequently increased intracranial pressure. Experimental and clinical evidence has been submitted by Dandy and others that occlusion of the great vein of Galen leads to internal hydrocephalus from overproduction of cerebrospinal fluid. It is suggested that moderate compression without complete occlusion of the vein is likely to give rise to increased intracranial pressure, accompanied by slight or neglible dilatation of the ventricles. If the views put forward have been correct the increased pressure caused by intracranial tumors is due to an excessive production of cerebrospinal fluid, the fluid being produced in such quantities that absorption cannot keep pace with production and the intracranial pressure being consequently raised.

Sarcoma of the Bladder.—CECIL (*J. Urol.*, 1926, **16**, 490) states that total cystectomy is indicated where the tumor is too large for resection or occupies a position not adaptable to resection. The position of these tumors is most frequently on the base, trigone or vesical orifice, though it is found more frequently on the lateral and anterior walls than epithelial tumors. The gross appearance is not characteristic enough to distinguish it from other tumors. Microscopically the tumors assume all the varieties of sarcoma. They have a great tendency to invade the surrounding structures, and are, moreover, of very rapid growth, not infrequently multiple. They have been found most frequently in the very young or those past middle age, but have been found at all ages. Diagnosis depends entirely upon a microscopic examination of the specimen. Hematuria is not constant and when present is usually a late manifestation. Other symptoms are also late to appear. Radiation has not been tried sufficiently to warrant a conclusion, but will most likely prove inadequate. While resection is the method of choice in early cases, in most cases total cystectomy offers the only chance of cure.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D.,

OF PHILADELPHIA.

Diphtheria Immunization in Providence.—SCAMMAN and POPE (*J. Am. Med. Assn.*, 1927, **88**, 563) in three years' experience Schick tested and immunized 15,000 children, and they feel that toxin antitoxin immunization eliminates approximately 90 per cent of the risk of contracting diphtheria in the immunized group. During this time 38 per cent of all the children in the age group five to nine years and 24 per cent of the children in the ten to fourteen years group were immunized. In the group under five years, in which the morbidity and mortality from diphtheria are practically at their height, hardly 4 per cent of the children have been immunized. They feel that to make immunization wholly effective some method must be devised to reach this susceptible group. The health department of the city is sending to the parents of every six months' old child a notice urging immunization by the family doctor or at a clinic. One benefit of diphtheria immunization which cannot be accurately measured is elimination of the spread of the disease by a reduction of the susceptible population. In the spread of a contact disease two factors are essential; cases or carriers of virulent organisms and susceptible contacts. If any increased proportion of the population is already immune, the probability of effective contact between each case of diphtheria and other persons is definitely decreased.

Two Hundred and Forty-three Fetal Autopsies: A Syphilitic Study.—MCCORD (*J. Am. Med. Assn.*, 1927, 88, 626) examined 243 infants at autopsy. Only 50 of these had been born alive, 189, or 77 per cent, were born dead and there were 4 abortions about the fourth month. There were 164 premature babies, or 67 per cent. Maceration was present in 45 per cent of the autopsies. Syphilis was positively demonstrated in 45 per cent of the cases; syphilis was probably demonstrated in 20 per cent of the cases. The causes of death in the order of frequency were: Syphilis, 57 per cent; brain hemorrhage and tentorial tears, 13 per cent; prematurity, 11 per cent; toxemia of the mother, 4 per cent. Bone lesion, known as Wenger's disease, seemed to be pathognomonic of fetal syphilis. The lungs, kidneys and liver seemed to be the tissues most frequently involved as evidenced by histologic changes. The spirochetes were found in the tissues in the following order of frequency: Lungs, kidneys and liver. The author feels that negative observations of any kind cannot absolutely exclude syphilis.

The Effect of Irradiated Milk on the Blood.—DAWKINS and PATTISON (*Lancet*, 1926, ii, 1314) feel that irradiated milk is a greater food value than non-irradiated milk. Their observations were made on five

children who had been in the hospital with active bone tuberculosis for an average period of four months without marked improvement in their general conditions or local lesions. During this period they were given ordinary hospital diet, which included cod liver oil and 1¼ pints of milk daily. Later ½ pint of this supply of milk was exposed daily to the rays of a quartz light at a distance of 2 feet for a half hour. The milk was contained in shallow trays and stirred frequently. There was no change in the other diet, but after four weeks the red cells and hemoglobin were found to have increased in four of the cases. The same amount of irradiated milk was continued and at the end of three more weeks the red cells had increased in every case, but the hemoglobin was only slightly changed.

Clinical Manifestations of an Enlarged Thymus.—MORGAN, ROLPH and BROWN (*J. Am. Med. Assn.*, 1927, **88**, 703) describe the clinical manifestations in 54 cases which they thought were due to disturbance of the thymic gland. Such symptoms as noisy nasal breathing, hoarse cough, attacks of syncope, restlessness and sleeplessness have not been previously described as being associated with thymic disturbance. The analysis of these symptoms strongly suggests that the cause of their protection is of a mechanical nature, and is most probably due to vagus stimulation. Roentgen ray therapy proved efficacious in relieving the symptoms in 96 per cent of these cases. This form of treatment if not carried to excess is unattended by danger. Recurrence of thymic enlargement or of clinical manifestations was noted in 12, or 22 per cent of the cases. In all these instances further Roentgen ray therapy resulted in complete recovery. Patients showing susceptible symptoms should be given the benefit of Roentgen ray therapy, even in the absence of positive Roentgen ray findings.

Pentosuria.—LEVY and PIERSON (*Am. J. Dis. Child.*, 1927, **33**, 212) report a case of pentosuria in a child aged three years. This is the youngest patient on record presenting this type of hereditary anomaly. It would seem that the supposition that the pentosuria was present at birth was accurate. The familial character of the disturbance coincided with other recorded instances. The exact nature of the metabolic disorder is purely speculative. The source of the pentose in this case was not in the diet because, with the exception of the first analysis of the urine, the amount of pentose was extremely constant in spite of dietary variation. Ten specimens examined in a course of about a month contained the following percentage of pentose: 0.24, 0.209, 0.185, 0.209, 0.178, 0.2, 0.209, 0.208, 0.172 and 0.263. The narrow limits in which the output of pentose fluctuated is interesting and there is suggested a comparison with the uniformity of the amount of cystin excreted in cystinuric subjects, which is remarkably constant, varying from 0.3 to 0.5 gm. per twenty-four hours. This is due to the failure of the body to utilize in its usual way some definite part of the protein metabolized. The relationship of pentosuria to diabetes mellitus cannot be dismissed lightly. In this case the pallor and loss of weight following an acute infection might lead one to suspect an existence of a true diabetes, and there was an unusually large output of urine. As a further point in this favor was the fact that the child improved on a diabetic diet together with the administration of insulin.

DERMATOLOGY AND SYPHILIS

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Syphilitic Paraplegia.—CHUNG (*Arch. Dermat. and Syph.*, 1926, **14**, 111) made an extensive clinical study of 34 cases of rapidly developing paraplegia of syphilitic origin, a rather common neurologic symptom complex in China. Two distinct groups are distinguished: (1) An acute type, which develops either overnight or within forty-eight hours, accompanied by a flaccid paralysis with total loss of sensory function below the lesion, with sphincter disturbances and vasomotor changes; (2) a subacute type, which develops more insidiously, associated more often with a spastic paralysis with increased reflexes, more or less disturbances in sensation, sphincter troubles and trophic changes. The pathologic condition underlying these lesions in the acute cases is always thrombosis of one or more important spinal vessels with secondary changes in the cord, and in the subacute cases is also one of thrombosis but with a more widespread meningomyelitis. Recovery is by no means rare. In general, the disease is not rapidly fatal; but the prognosis as to function in protracted cases is grave. Reëstablishment of the circulation is largely responsible for the cases of recovery. The use of arsphenamin is necessary to cure the underlying syphilis and to prevent, if possible, further damage to the nervous system.

Vascular Reactions of the Skin to Injury: Some Effects of Freezing of Cooling and of Warming.—In conducting an experimental study of freezing and heating of the skin under controlled conditions, LEWIS and LOVE (*Heart*, 1926, **13**, 27) find that the skin begins to freeze when its surface temperature is reduced to a point lying between −2.2° and −25° C. As a result of supercooling the skin may be induced to tolerate a temperature as low as −20.4° C. and a subcutaneous temperature of −9°. Wetting the skin abolishes the supercooling capacity and causes more rapid freezing. Supercooling may occasionally lead to wheal formation, but rarely injures the skin, and skin will show a great increase in capacity for supercooling (that is, tolerance of cold) if it is kept unwashed for some days. (This probably rationalizes from the physiologic standpoint the extraordinary tolerance of certain strata of society for cold.—Rev.) In a further study of livido racemosa and of the response of the cutaneous capillaries to heat, the author (*Heart*, 1926, **13**, 153) and his coworkers have advanced the interesting theory that types of telangiectasia in which no histologic abnormality is found are the result of a prolonged or permanent functional vaso-

paresis, such as can be induced by exposure to heat (in the case of livido calorica) rather than to compensatory dilatation of vessels in response to obliteration of others, such as is observed histologically in certain types of telangiectasia.

OBSTETRICS

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A Summary of the Midwife Situation in Pennsylvania.—A complete summary of the situation dealing with the midwife problem is given in NOBLE'S article (*Atlantic Med. J.*, 1926, **30**, 67). The Department of Health undertook the supervision and instruction of these women in eight counties of the State, by permission of the Board of Medical Education and Licensure. The work began in 1922, and was met with difficulties, misunderstanding and resentment; added difficulties were met when the futile Pennsylvania Law, which provides that midwives shall deliver only uncomplicated vertex cases; for any deviation from this rare occurrence the midwife must call a physician. Classes of instruction were given the midwives, consisting of manikin demonstration; there are on record 21,763 deliveries; of these, there were 40 maternal deaths, 611 infant deaths in the first month of life. Most of the work has been done with the foreign population, and the midwives have organized themselves into leagues, fostering pride in their profession. Unless our Immigration Laws change and a large influx of foreigners occurs the midwives will gradually disappear; few new licenses are being granted, and the author states that in all probability the entire group will probably automatically be eliminated in the not too distant future.

Chronic Endocervicitis.—MILLER (*J. Am. Med. Assn.*, 1926, **87**, 1695) goes carefully into the embryologic and histologic formation and structures of the cervix, and the function of the cervix is clearly out lined. The importance of endocervicitis and the intrinsic origin along with the multiple clinical findings make this a common gynecologic condition. It must be emphasized that the complicated structure of the cervix, particularly in the light of its frequent exposure to trauma and external infection, make it an ideal location and medium for the growth of bacteria. The etiology is still far from clear. A certain proportion of cases can be attributed to the following: Specific infec-

tion from direct contact, unnoticed childhood infections which have laid dormant for years and to the gonococcus. Much attention has been called to arthritis, nervous and mental diseases and other conditions which have been attributed to the disease of the cervix. Faulty instrumentation, extension of infection upward, following menstruation, chronic constipation, anemia and tuberculosis are among the predisposing factors. Of the infections, all types of bacteria may be identified. Certain types are predominant; of these the gonococcus is most common; streptococcus, the staphylococcus and the colon bacillus are generally agreed to be among the chief bacteria causing the infections. The most constant symptom is leucorrheal discharge. The pathologic picture is for the most part typical. The cervical mucosa appears red, edematous and everted; areas of granular proliferation are adjacent to the external os. The whole is covered with a thick, mucopurulent discharge. Parametritis, posterior cellulitis and sensitive, tender ovaries may be found among a certain percentage of cases. The cervix has been called the tonsil of the pelvis, and much investigation has been undertaken with the idea of identifying it as a systemic focus of infection.

The Clinical Significance of Roentgen Ray Pelvimetry.—THOMS (*Am. J. Obst. and Gynec.*, 1926, **12**, 543) points out the principles of the methods used by him and published in 1922, since simplified and improved. The position of the patient and the degree of divergence through which the Roentgen ray passes to the plate is shown. The method is outlined in each step with the patient in the proper position and sketches shown and the Roentgen ray technique is included. This method of Roentgen ray pelvimetry is simple and adds materially to the external diameters and pelvic measurements of the routine pelvimetry in pregnancy, giving us a remarkably accurate measure of the superior strait as well as the other pelvic diameters. The lateral view is of great importance, particularly in deformities of the pelvis. The author so describes the technique that any competent roentgenologist could easily apply it, aiding materially the obstetrician in the diagnosis as well as pelvic measurements.

The Occipitoposterior Position.—A summary of the frequency of this condition and the importance of keeping it before the medical profession until it is better understood is given clearly by BARNES (*Am. J. Obst. and Gynec.*, 1926, **12**, 734). As to its frequency as a primary condition there is a wide variance of opinion. The percentages range from 11 to 70 per cent. The problem of the occipitoposterior brings out many methods of delivery and multiple difficulties in handling these cases. The occipitoposterior position is often overlooked, the etiologic factor, the early diagnosis by abdominal palpatation and the correct procedure of handling these cases is clearly given to us. The outline of the different methods of treatment and management of these cases is given in detail. Version, rotation, manual and instrumental, Scanzoni method, special instruments are elaborated and the pitfalls and dangers are fully explained.

GYNECOLOGY

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Operative Treatment of Cancer of the Cervix.—There are few clinics in this country which have issued reports in recent years on the operative treatment of cancer of the cervix, since radium has largely replaced operation as the therapeutic measure of choice. In Germany, however, there are still a number of surgeons who prefer operation. A report from the clinic of Franz, in Berlin, has been presented by WILLS (*Zentralbl. f. Gynäk.*, 1927, **51**, 18), who states that infiltration of one or both parametria is not a contra-indication to operation, provided the bony pelvic wall is not involved, and extension of the cancer to the vaginal walls is not considered a contra-indication. Cancerous invasion of the bladder precludes operation because experience has taught that resection of the involved bladder wall is practically always followed by early recurrence and in many cases by incurable bladder fistulas. There are several constitutional conditions which may contra-indicate operation, such as marked obesity, diabetes, cardiac disease and the age of the patient; in fact, since 1919 no patient over sixty-five years has been operated upon in this clinic. The average age of their patients during the reported five years was forty-four years and one and a half months. During this period Wertheim operations were performed upon 296 women, of whom 12 were sixty years or older. Of these 12 there was a 50 per cent mortality and only 1 of the patients lived four years after the operation. Of the entire series the carcinoma was confined to the cervix in only 15.5 per cent. The primary mortality averaged a trifle over 14 per cent and 133 of the patients (44.93 per cent) were alive after five years. If only the early cases are considered the primary mortality was 6.5 per cent and 76 per cent of the patients survived five years, while the mortality of the borderline group was 29 per cent. There were 4 patients in the series who were pregnant in addition to having carcinoma, and it is their belief that the carcinoma should be operated upon as soon as possible without regard for the pregnancy unless the carcinoma is inoperable and the pregnancy is older than thirty-five weeks, in which event the end of gestation should be awaited. In the 4 cases in this series (pregnancy at two, three, five and eight months) the radical Wertheim operation was undertaken in all; in the last case, after the child was delivered by Cesarean section, the mother dying of peritonitis. Two of the other patients died of recurrences, while the fourth patient is free from recurrence after seven years. The vaginal operation of Schauta has been performed only twelve times during the period reported. They

feel that it has a very limited place in the treatment of cervical cancer, and should be reserved for the obese and aged patients. The following table which briefly shows the results obtained in this clinic by means of the Wertheim operation will be of interest:

Year.	No. of operations.	Primary mortality.	Alive after five years.
1916	45	5 (11 per cent)	17 (38 per cent)
1917	38	3 (8 per cent)	18 (47 per cent)
1918	84	15 (18 per cent)	31 (37 per cent)
1919	63	9 (14 per cent)	30 (48 per cent)
1920	66	10 (15 per cent)	37 (56 per cent)

Bilateral Pyelograms.—Most gynecologic urologists have been hesitant about making pyelograms of both kidneys at the same time because of a fear of possible serious renal impairment. This fear is not justified according to MATTES (*J. Am. Med. Assn.*, 1927, **88**, 17), who describes his results with the use of 40 per cent sodium iodide solution by what he terms the "flat sac method." According to his technique no purgatives or enemas are ordered so as to avoid any tendency to reflex irritative phenomena. The use of small catheters permits of lateral drainage, does not block the ureter and does not disturb the waves of contraction, particularly in cases of ureteral strictures and ptosed kidneys. The high concentration of the solution permits dilution by the urine, without affecting its ability to cast a shadow. The catheters are passed to the pelves, or as far as they will go. Each side is aspirated and the amount of fluid withdrawn noted. A plain picture is first made showing the course and relations of the catheters. The second roentgenogram follows the injection of each pelvis with from 3 to 4 cc. of fluid. If any pain is elicited or any symptom noted the injection is discontinued on that side and an approximate amount instilled on the opposite side. The catheters are plugged during the taking of the pyelogram. The cause of any reaction may be due to the catheter end being in the calix, to the unusual smallness of the pelvis, to some pathologic condition or to a contraction of the pelvis during the moment of the injection. The instillations are made fairly rapidly, within from four to eight seconds. The points that he emphasizes are that the capacity of the renal pelvis is small and that if small catheters are used and the injections quickly made, using a high concentration solution, there is very little danger in making simultaneous bilateral pyelograms.

Relation of Nerve Supply to Ovarian Function.—In his endeavors to determine the relationship, if any, between the nerve supply and the function of the ovary MACOMBER (*Boston Med. and Surg. J.*, 1927, **196**, 21) performed two sets of experiments upon rats. In the first experimental study the nerve to one ovary was divided and a section of the nerve removed, while in the second set of experiments sections of the nerves to both ovaries were removed. These animals were then bred and the effects upon fertility were noted. The results proved conclusively that the nerve supply to the ovary is not necessary to the function of normal reproduction. They also show that the sterility produced by dividing the ovarian artery, veins and nerves in a previous set of experiments was not due to any interference with the nerve

supply. Previous experiments in which the ovarian artery alone was divided without producing any notable amount of sterility had shown that the interference with the arterial circulation alone could not be considered responsible. By exclusion, therefore, this experimental sterility would seem to be due to some interference with the venous return from the ovary. Such a supposition is the more reasonable to the author, as it is well known in human surgery that interference with the venous circulation will often lead to the development of a cystic condition in the ovary.

OPHTHALMOLOGY

UNDER THE CHARGE OF

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Interstitial Keratitis of Dental Infection Origin, with the Report of an Interesting Case.—MACKENZIE (*Med. J. and Record*, 1927, **125**, 85) reports the case of a man, aged sixty-four years, who had a severe and painful, nonsuppurative keratitis and iritis of the right eye, which had been diagnosed as interstitial keratitis and treated as such by antiluetic remedies for five weeks by an ophthalmologist, with no results. There was a loss of the normal transparency of the cornea due to the presence of a grayish infiltration in the corneal stroma covering approximately half of the cornea. The deepest infiltration was in the center of the cornea, leaving the periphery fairly clear. The left eye was not affected nor were there any stigmata of hereditary lues. Several alveolar abscesses were found by Roentgen ray in edentulous areas. After surgical treatment had successfully cleared these areas of infection the ocular inflammation subsided and the cornea gradually became clearer, with vision equal to 6/10. The author states that "interstitial keratitis, which is generally assumed to be of syphilitic origin, can be due in rare cases to a focal infection." Interstitial keratitis of syphilitic origin is practically always bilateral, whereas when due to focal infection it is generally unilateral.

Keratitis as a Complication of Dengue Fever.—RICHARDSON (*South Med. J.*, 1927, **20**, 32) observed three cases of keratitis, a rare complication of dengue fever, the first symptom of ocular complication of hyperesthesia of the cornea. After the first few hours of hyperesthesia the affected area of the cornea becomes anesthetic, and this anesthesia persists for some time, in one case more than two months. In the cases in which the keratitis developed during the attack of fever, the superficial ulceration was more extensive and the iris very irritable, requiring the continued use of a mydriatic. Postdengue keratitis is evidently due to peripheral neuritis of the portion of the corneal nerve plexus corresponding to the affected area, with resulting keratitis neuropara-

lytica. Ocular symptoms prominent in the active stage are intense aching of the eyeballs, supraorbital neuralgia, sensation of tension within the globe, pain with ocular movement, lacrymation, photophobia and burning sensation of the conjunctiva. Blepharospasm is associated with mild or severe injection of the conjunctiva. Bacteriologic examination of the secretions of the conjunctiva are negative. Intraocular tension is normal. Pupils and pupillary reflexes are normal. Three cases of unilateral herpes of the eyelids were seen in the same group of dengue fever cases. In addition, two of these showed herpes of the lips and one of the alæ of the nose. In a discussion of this paper, Gill stated that ocular complications of dengue fever are as follows: (1) Retrobulbar pain considered due to myositis of the extraocular muscles, present in every case; (2) conjunctival congestion or suffusion of varying degree, always present; (3) congestion of retinal veins thought to be due to cerebral congestion; (4) weakness of accommodation resembling that after diphtheria, but of shorter duration. No extraocular paralyses were found in 1241 cases, nor was there a case of keratitis in the group.

OTO-RHINO-LARYNGOLOGY

UNDER THE CHARGE OF

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Radium in Polypoid Ethmoiditis.—Among the diseases encountered by the rhinologist, one of the least amenable to treatment is hyperplastic ethmoiditis with polypoid change. While the etiology of this condition is still in question it is generally conceded that irritation plays an important rôle, but it has not been determined that it is the predominant one. McCULLAGH and ROBINSON (*Arch. Otolaryngol.*, 1926, 4, 215) believe that ethmoidal polypi seldom develop in cases that are frankly purulent from the start; they call attention to the frequent association of asthma with ethmoid disease as an added factor which should be a further incentive to stimulate search for a truly causative agent. Formerly the sole method of attack has been surgical, the results having been gratifying neither to the patient nor to the surgeon. The authors have supplemented the surgical procedure—performed as completely as possible—with the introduction of radium. The radium is inserted into the ethmoidal area in a tube (50 mg. for two hours or 100 mg. for one hour) and repeated within ten days or two weeks. The dosage varies in the individual case, the average condition receiving four applications, or approximately 400 mg. hours. The gamma rays are used, the beta rays being screened off by 0.2 mm. platinum and 1 mm. brass. Sixteen cases were so treated, 12 of which had a preliminary complete ethmoidectomy. All patients were markedly benefited subjectively, although the authors do not claim a definitive cure

in any. They believe their experiences with this method corroborate the conclusions of the reports of Sluder, and of Lyons, both pioneers in this field.

Nonendoscopic Cases of Foreign Bodies in the Tonsil.—"Among the many foreign bodies found in the faucial and lingual tonsils and in the lymphoid tissues of the pharynx, fish bones are more common than all the other forms combined. Other substances, such as toothbrush bristles, toothpicks or slivers of wood, spicules of some of the long bones, plant stems and occasionally some form of metallic foreign bodies, are found." In his dissertation upon this subject, CLERF (*Arch. Otolaryngol.*, 1926, **4**, 489) states that it is safe to assume that carelessness in the preparation and in the eating of food is the most important factor in their occurrence. According to Jackson, carelessness is responsible for the presence of foreign bodies in the air and food passages in 87.2 per cent of cases. Individuals wearing complete dentures, which deprive them of the protective sensations of the parts they cover, frequently are afflicted with foreign bodies. Rapid eating, with bolting of food, and hypertrophic and protruding tonsils predispose to foreign body lodgment. Sharp, sticking pain, intensified by swallowing, is a prominent symptom. Although the power of localization about the tonsil region is poor, it is useful in determining the side affected. Diagnosis depends on the history and a thorough, systematic search, using an angular pillar retractor. If inspection fails, palpation is a valuable adjunct. Roentgenology is invaluable if the foreign body is in the esophagus or the hypopharynx. Removal by forceps, followed by colloidal or inorganic silver applications, constitute the treatment. In cases where the foreign body has been proved to be buried in the tonsil, tonsillectomy should be done.

The Alkaloids of Ceanothus Americanus and their use in the Control of Hemorrhage in Laryngology.—Although reference to the use of Ceanothus americanus as a "styptic for restraining hemorrhage from wounds" has been found as far back as 1836, and the work of CLARK (*Am. J. Pharm.*, 1926, **98**, 147) indicated several distinct advantages of this drug over others now in general use as hemostatics, PAYNE (*Ann. Otol., Rhinol., and Laryngol.*, 1926, **35**, 769) was unable to find "any work in the literature covering the clinical observation of this drug as a coagulant." Accordingly, he reports his observations of a standardized solution containing 1 mg. of the mixed alkaloids of Ceanothus americanus per cubic centimeter on the coagulation time of 234 cases, most of whom received a dose of 15 cc. by mouth. The coagulation time of the blood was determined by the capillary-tube method. Following the oral administration of the solution there was a consistent depression in coagulation time, amounting to an average of 21.9 per cent in 225 cases in which the clotting time was normal or low. The shortening of the coagulation time began within fifteen minutes after the administration of the solution and reached its maximum in about forty-five minutes. Age or sex of the patient did not influence the coagulant action of the drug. In 8 instances whose average coagulation time was 9.68 minutes the average reduction in clotting time was 50.6 per cent within an hour after the drug had been given. There was practically no postoperative bleeding in these cases.

RADIOLOGY

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Roentgenologic Diagnosis of Disease of the Uterus and Adnexa.—NAHMMACHER (*Fortschr. Roentgenol.*, 1926, **35**, 579) has employed uterosalpingography with iodopin in fifty cases, and writes with enthusiasm of its value, not only in the diagnosis of sterility but of many other conditions. His illustrations are numerous and striking. In metritis the uterine cavity is greatly enlarged with smooth contours, and the cervical canal is broadened. Polyps and submucous myomas produce characteristic filling defects in the iodopin shadow. In ovarian tumor the mass is surrounded or partly surrounded by the tube and the uterus is displaced. The picture of uterus bicornis is characteristic. Employment of the method is contraindicated by acute inflammations, fever, pregnancy and gonorrhea, but not by hemorrhage.

Family Diverticulosis of the Colon.—MACKOY (*Radiology*, 1926, **7**, 408) reports 8 members of a family, in three generations, who suffered from a chronic intestinal trouble which presented similar clinical pictures in all cases. By Roentgen ray examination the diagnosis of diverticulitis of the colon was established in 2 of the cases (sisters) and a symptomless diverticulosis was demonstrated in a third sister. In 1 of the 3 patients more than 100 diverticula of various shapes and sizes were revealed.

Diagnostic Inflation of the Knee Joint.—BERNSTEIN and ARENS (*Radiology*, 1926, **7**, 500) describe a method of inflating the cavity of the knee joint with carbon dioxid for roentgenography. They feel that the method is of substantial aid in the diagnosis of tears of the ligaments, displacements and tears of the cartilages and chronic synovitis. They have employed it in about fifty cases without untoward results.

Roentgenologic Diagnosis of Congenital Disease of the Heart.—ARKUSSKI (*Fortschr. Roentgenol.*, 1926, **35**, 455) believes that every congenital cardiac lesion has a certain corresponding Roentgen picture. In a case of open ductus Botalli the roentgenogram revealed a characteristic hypertrophy of the left ventricle with protrusion of the arch of the pulmonary artery. In a case of stenosis of the pulmonary artery the right ventricle was enlarged and the arch of the artery was flattened. The clinical diagnosis of patent ductus Botalli was shown to be erroneous in one case, the actual lesion being pulmonary tuberculosis, and in another patient the diagnosis of defect in the ventricular septum was disproved, luetic mesaortitis being found.

Roentgen Therapy of Syringomyelia.—STORMER and BREMER (*Fortschr. Roentgenol.*, 1926, **35**, 547) report the results of Roentgen therapy in 9 cases of syringomyelia. Improvement was marked in 3 patients, 3 were slightly improved and 3 remained unchanged. Thirty per cent of the erythema dose was given, and repeated twice at intervals of two or three days, followed by another series after five weeks.

Resolution in Pneumonic Consolidation.—ALLISON (*Am. J. Roentgenol. and Rad. Therap.*, 1926, **16**, 549) quotes with approval Giffin's opinion expressed twelve years ago as to the great accuracy of the Roentgen ray in excluding pulmonary tuberculosis. The author feels also that with the Roentgen ray more early tuberculosis is recognized now than ever before, but he believes, nevertheless, that the percentage of nontuberculous lesions diagnosed with the Roentgen ray as tuberculous is higher than it was ten years ago. The earliest Roentgen sign diagnosis of tuberculosis is the typical mottling first described by Cole. Signs are present at an earlier stage than this but they are not pathognomonic. Remarkable resolution, even to complete disappearance of a tuberculous lesion, can take place in a very few months.

Diseases of the Chest Demonstrated by Lipiodol.—PIRIE (*Am. J. Roentgenol. and Rad. Therap.*, 1926, **16**, 553) has had experience with seventy-seven injections of lipiodol into the lungs for roentgenologic examination. No ill effects followed save in one instance, a patient who had advanced bilateral tuberculosis with pneumonia, and who died of acute cardiac dilatation during injection. Lipiodol produces a pathognomonic Roentgen picture in bronchiectasis. Among other conditions in which its employment is indicated are: Suspected tuberculosis when bacilli cannot be found, after thoracoplasty, for demarcation of the diaphragm in suspected subdiaphragmatic abscess, for localization of a known pulmonary abscess, for stenosis, for bronchopleural fistula and for foreign bodies. In skilled hands bronchoscopic injection of lipiodol is the best method.

NEUROLOGY AND PSYCHIATRY

UNDER THE CHARGE OF

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Idiopathic Narcolepsy.—ADIE (*Brain*, 1926, **49**, 3), writing on this interesting subject, begins his article with the definition, "a disease characterized by the occurrence of attacks of irresistible sleep without apparent cause, and curious attacks on emotion in which the muscles relax suddenly, so that the victim sinks to the ground fully conscious

but unable to move." The author bases his description of this disease upon an analysis of 6 of his own cases as well as upon 15 cases previously reported. He feels that true narcolepsy is a distinct disease and objects to considering this disease as an epileptic or as a functional condition. He gives excellent case histories that bring out the following facts regarding this disease: (1) Sex, duration and treatment; narcolepsy is especially confined to the male sex—17 cases occurred in this sex to 3 in female sex. (2) Age at onset varied from thirteen and a half to thirty-nine years. The usual statement that this disease always begins at puberty is incorrect, according to the author. The duration of the disease varies from six months to twenty-one years. All forms of treatment have been tried without success, including the use of the bromids, thyroid extract, caffein and other drugs to prevent sleep. Hospitalization made the attacks less frequent, although they recurred with original frequency after discharge. In regard to the family history, there is no evidence that heredity plays an important factor. In general, the patient's mental conditions were normal. The laboratory examinations, including spinal fluid examinations, were normal. Two kinds of attacks occur, the sleep attack and cataplexy. The sleep attacks varied in duration from a few seconds to forty minutes. The patients passed into a condition resembling normal sleep and were usually easily awakened. Attacks occurred while the patient was walking, riding or cycling, on the march, during bombardments. One patient fell asleep driving his car. Another patient fell asleep while dancing. Auræ often occurred, consisting of fatigue and discomfort in frontal region. Some patients can resist the inclination to sleep. Attacks vary in frequency from two to three per day. The cataplectic attack may be brought about by any emotion, especially by hearty laughter and anger. Attacks occurred in the anticipation of enjoyment, especially in the theater. The patient's limbs become flaccid and he falls, unable to talk, without losing consciousness. Cataplectic attacks can be avoided by refusal to laugh. Cataplexy in narcolepsy is as characteristic of the disease as the sleep attacks. The author differentiates this disease from epilepsy, pyknolepsy, hysteria and all other diseases in which excessive sleep occurs. Narcolepsy should never be used as a symptom of many dissimilar conditions. True narcolepsy may follow an attack of encephalitis lethargica. The combination of sleep attacks and cataplexy, with the above exception, does not occur in any other condition. Narcolepsy is considered by the author to be a disease of the pituitary and adjacent vegetative centers in the floor of the 'tween-brain which form an endocrine nervous system. He discusses Pavlow's conception of normal sleep and produces evidence to support the above localization.

The Constancy of the Intelligence Quotient of Mental Defectives.—A study and reëxamination of 441 feebleminded persons who had been inmates of an institution for periods varying from two to ten years made by MUROGNE (*Ment. Hyg.*, 1926, **10**, 751) showed a marked constancy in their intelligence quotient. In 72 per cent of the cases no change was noted. In 24 per cent there was a loss and in 5 per cent a gain. Ninety-one per cent showed a variation of no more than 10 points. The greatest frequency of variation was in children under

twelve years of age. Males show more variation than females and their change tended to be a loss. No explanation of the variations appeared in these studies.

A Note on Type of Onset in Relation to Clinical Type in General Paresis.—BUNKER (*Am. J. Psychiat.*, 1926, **6**, 119) states that very little correlation exists between the type of onset and the clinical type of general paresis which develops with the exception of the "manic" cases. In a study of 74 cases of general paralysis, 57 first showed abnormalities in the emotional sphere in one of two forms—either as irritability or a seclusive apathetic reaction. All of the "manic" cases developed from those individuals having an "irritable" type of onset. Early loss of weight, increased tendency to sleep and in some cases forgetfulness were without significance as to the subsequent clinical type (dementing simple or "manic"). Of 11 patients with early speech defects, all but 1 fell in the category of simple dementing cases.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Basic Concepts of Immunity.—The Ehrlich theory as to the origin and nature of antibodies has had wide acceptance and, although frequently attacked as fantastic, the terminology of immunologists would indicate that this hypothesis is still largely held. MANWARING (*J. Immunol.*, 1926, **12**, 177) believes it would be wise if we would quietly lay aside for future reference the entire scheme of immunology based upon the specific receptor hypothesis, and considers it probable that the prominence given to this theory constitutes today our most serious handicap to immunologic progress. The mystery of the origin and nature of antibodies may be unraveled by directing attention to the normal and pathologic permeability of fixed tissues and wandering cells for immunologic antigens and to the interplay of antigens with extracellular and intercellular, hydrolyzing and synthesizing enzymes. Physiologic facts developed in his laboratory suggest that the fundamental Ehrlich concepts are at least problematic. There is no direct experimental evidence either for or against the three major hypotheses of the Ehrlich theory, but the indirect experimental evidence is contrary to certain deductions logically drawn from the theory. The fixed tissues of an immune animal, freed from circulating antibodies, should

necessarily be hypersensitive, due to an increased number of sessile receptors. This was not found to be true by experimental test and similarly with a number of other deductions. The author thinks that a consistent theory of immunity may be based on the assumption that antibodies are slowly synthesized in the body by the action of synthesizing enzymes, and by them specifically adapted to injected antigens or to products of antigen hydrolysis. Such an assumption is more nearly in accord with the known facts of cellular biology, and it would, also stimulate the hope that in time therapeutic antibodies may be successfully synthesized in the chemical laboratory.

Pulmonary Neoplasms.—ATKINSON (*Am. Rev. Tuberc.*, 1926, **14**, 556) concludes that primary malignant tumor of the lung has increased decidedly in recent years, and this increase is out of all proportion to the general increase in cancer incidence. Heretofore, lung neoplasms have not offered a fertile field for treatment because only secondary tumor deposits have ordinarily been recognized, and when primary neoplasm has been diagnosed the growth has usually been so far advanced as to offer little chance for successful attack. Lung tumors are most frequently diagnosed as tuberculosis. Since pulmonary malignant tumor is now known to be definitely on the increase, special efforts should be put forth to detect the condition at an early stage.

Information on Streptococci.—Recognizing that there are many divergent views on the differentiation, transmutation and virulence alteration of streptococci, WIRTH (*Centralbl. f. Bakteriol.*, 1926, **99**, 266) undertook a careful study of some twenty tests on 171 strains of streptococci, including pneumococci. By these tests he divided his cultures into eight different types, and with the characters thus determined he studied the hemolysis on blood agar and the mouse virulence, both of which were found to be capable of alteration. He does not consider that there has been reported up to date a single example of unequivocal transmutation of one type of streptococcus into another type. The bactericidal test, using blood of healthy humans, was found to indicate the relative virulence of his strains for mice. He could not, however, confirm the work of Ruge, Philipp and others, who claimed that the multiplication of a strain of streptococcus in the blood from a patient indicated an unfavorable prognosis. His work dealt with infections of the throat and ear, while the others had to do particularly with the genital tract. On the other hand, the local injury of tissue he believes to be the determining factor in the prognosis, since damaged tissue was found experimentally to increase the virulence of injected hemolytic streptococci, and the mere presence in an infected site of streptococci, capable of growing in the blood of a healthy or diseased person, does not in itself indicate what the outcome may be. This is a valuable contribution to the study of streptococci.

Experimental Production of General Peritonitis.—STEINBERG (*Am. J. Path.*, 1926, **2**, 415) states that there are three general methods employed to produce experimental peritonitis: (1) Intraperitoneal injection of microörganisms; (2) perforation of bowel; (3) ligation of appendix. White rats, guinea pigs and rabbits succumb rapidly to

intraperitoneal injection of fairly virulent bacteria, while cats and dogs do not. But when gum tragacanth is added to a culture of Bacillus coli and injected intraperitoneally into dogs, they succumb. Ligation of the appendix produces death in forty-eight hours in the majority of animals. The author and Ecker seldom found any pathologic changes in the peritoneum of rabbits receiving Bacillus coli antiserum intravenously and then given Bacillus coli intraperitoneally. But Bacillus coli antiserum and an equal amount of twenty-four-hour Bacillus coli broth culture mixed, and injected intraperitoneally into rabbits, produced acute and healing peritonitis. The free peritoneal exudate contained fibrin and a great many polymorphonuclear leukocytes, but the fixed tissue reaction was predominantly mononuclear in type. Benians injected rabbits intravenously with small numbers of Bacillus coli to produce active immunization, and found that subsequent intrapleural injection of a lethal dose of Bacillus coli produced no ill effects.

HYGIENE AND PUBLIC HEALTH

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Measles Prophylaxis.—TOWNSEND (*Boston Med. and Surg. J.*, 1926, **194**, 869) used prophylactic measures in an epidemic of 63 cases of measles in a boarding school of 400 boys. A dosage of blood from an adult who had had measles twenty years previously appeared to have no effect in preventing or modifying the disease. Blood from convalescents had little or no effect in preventing infections, but markedly influenced the course of the disease when given before the end of the first week of the incubation period. Thirty-two cases inoculated with convalescent blood at least eight days before development of the rash showed an average duration of the febrile period of 3.66 days, with a maximum temperature of 102.5°, whereas 21 boys who received no inoculation showed an average duration of the febrile period of 6.45 days and a maximum temperature of 103.5°. The average stay in the infirmary of the 32 inoculated boys was 9.7 days, whereas the average stay of the control group was 13.6 days. The mild character of the disease in many of the boys who were inoculated was very evident and among them absolutely no complications occurred, while in the control group of 21 there was 1 case of bronchopneumonia, 1 of otitis media, 1 of frontal sinusitis and 1 of external otitis. The inoculations had no ill

effects whatever. Beneficial effects were obtained whether the blood was administered as late as six days after exposure or as early as twelve days before the probable date of infection.

The Relation of Endemic Goiter to Certain Potential Foci of Infection.—OLESON and TAYLOR (*Pub. Health Repts.*, 1926, **41**, 557) give the following summary and comments: (1) Examinations were made of the teeth and tonsils of 1341 white boys and 1576 white girls in eight schools in Cincinnati for the purpose of determining whether there was a relationship between potential foci of infection and thyroid enlargement. (2) Records were kept of slight and marked thyroid enlargements as well as of slight and marked decay of teeth; in addition, there were recorded the number of apparently normal tonsils, the absence of tonsil through operation, hypertrophy and cryptic degeneration. (3) Slight thyroid enlargements prevailed to the extent of 37.2 per cent among the boys and 50.4 per cent among the girls; both moderate and marked enlargements were approximately seven times more prevalent among the girls than among the boys. (4) In the group studied slight and marked dental decay is no more characteristically associated with thyroid enlargement than with normal thyroid status; furthermore, the degree of thyroid enlargement appears not to be dependent upon the amount of dental decay. (5) Normal tonsils were found more frequently among both boys and girls with thyroid enlargement than among those with normal thyroids. (6) Approximately one-third of the children examined had had their tonsils removed by operation; a slightly greater percentage of thyroid-normal children had had their tonsils removed than those in whom the thyroid was enlarged at the time of the examination; while differences may be noted in the several age groups as regards absence of tonsils, removal often being associated with a higher percentage of thyroid-normal individuals, the evidence is suggestive rather than striking. (7) Enlargement of the tonsils was found more frequently among boys and girls without thyroid enlargement; while some of the evidence concerning hypertrophy of the tonsils in the several age groups is suggestive, the data are too uneven in trend to be convincing. (8) There was no consistent evidence of correlation between cryptic tonsils and thyroid status. (9) Marked thyroid enlargements among the girls are not associated with enlarged or cryptic tonsils as often as are slight thyroid enlargement. The size of the thyroid enlargement is probably independent of tonsillar or dental conditions. (10) Based upon the material gathered during the present investigation, it is believed that there is no definite relations between thyroid status and potential foci of infection presumably located in decayed teeth and enlarged or cryptic tonsils. Comment: The number of children included in the present survey was small and the observations were subject to manifest limitations. Before the relationship between thyroid enlargement and potential foci of infection in the teeth and tonsils can be regarded as definitely determined it is desirable that additional studies be made in other sections of the country on a more comprehensive scale and possibly with different methods. Nevertheless it is felt that in so far as the present study is concerned, such a relationship is nonexistent. Despite these negative findings, neglect of oral hygiene is not advocated. On the con-

trary, renewed efforts to insure as nearly perfect denture as possible, through appropriate nutritional guides and practice, as well as competent dental prophylaxis and treatment, are recommended and urged. Moreover, appropriate treatment for enlarged and diseased tonsils is likewise advised.

PHYSIOLOGY

PROCEEDINGS OF

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SESSION OF MARCH 21, 1927

The Production of Heterophile Antibody by Acid-fast Bacteria.—J. D. ARONSON and C. F. ARONSON (from the Henry Phipps Institute, University of Pennsylvania). The serum of rabbits injected with suspensions of the organs of guinea pig, horse, dog, cat, mouse or turtle will hemolyse sheep cells. On the other hand the serum of rabbits injected with the suspension of the organs of rabbit, sheep, goat, man, ox or rat lack this property.

The antibody produced by the injection of the organs of the first group of animals has been termed heterophile antibody while the antigen has been termed heterophile antigen.

The heterophile antigen is soluble in alcohol and is not affected by prolonged boiling. It gives a positive complement reaction with heterophile serum and produces a precipitate with the serum. The alcohol soluble fraction is the specific fraction of the antigen but when injected into animals does not produce heterophile antibody. The addition of protein to this fraction is essential for the production of heterophile antibody.

Heterophile antigen has been found in *B. dysenteriæ* (Shiga), and in one of twelve strains of *B. lepisepticum.*

In this study the occurrence of heterophile antigen in the various acid-fast bacilli was determined. Immune sera were prepared by repeatedly injecting rabbits, intravenously, with suspensions of the various acid-fast bacilli. The animals were bled to death ten days after the last injection and the sera collected and heated at 56° C. during thirty minutes. The amount of heterophile antibody present in the various sera was determined by adding to various amounts of the different sera two units of fresh guinea pig complement and 0.1 cc. of a 5 per cent suspension of sheep cells. Readings were taken after thirty minutes incubation and again after standing overnight in the ice box.

No heterophile antibody was present in the serum of the rabbits which had been injected with the human, bovine or avian type of *M. tuberculosis* or with the following acid-fast mycobacteria: *M. lepræ* (Clegg), *M. lepræ* (Duval), *M. lepræ* (Kedrowski), *M. butyricum,*

M. "milk," M. butter (Korn), *M. butter Rabinowitch, M. Rabinowitch, M. smegmatis, M. mist, M. paratuberculosis, M. pseudoperlsucht, M. marinum, M. chelonei, M. marpman.* On the other hand the serum of the rabbit immunized with a culture of *M. phlei* was found to hemolyze sheep cells in a dilution of 0.001 cc. to 0.0005 cc. The heterophile nature of this antibody was further studied by means of the complement-fixation reaction and by absorption experiments. It was found that the serum gave a positive complement-fixation reaction with an alcoholic extract of guinea pig kidney but the reaction was negative when alcoholic extract of beef heart was used. The heterophile antibody present in the immune serum of *M. phlei* was absorbed by unheated and heated sheep cells but not by unheated or heated human cells.

An experiment was carried out to determine whether heterophile antigen is produced by acid-fast bacilli when grown on Long's synthetic medium. Cultures of *M. phlei, M. lepræ* (Clegg), *M. milk* and *M. paratuberculosis* inoculated on this medium and incubated during two weeks were filtered through filter paper and the filtrate treated according to the method of Hopkins and Pincus for crystallizing egg albumin. The resulting precipitate was dialyzed and rabbits were injected repeatedly with the nondialyzable residue. In the serum of the rabbits injected with the nondialyzable residue of *M. phlei, M. milk* and *M. lepræ* (Clegg) no heterophile antibody was found while the serum of the rabbit injected with the nondialyzable residue of *M. paratuberculosis* in a dilution of 0.001 cc. to 0.0005 cc. hemolyzed sheep cells. This serum gave a positive complement-fixation reaction with an alcoholic extract of guinea pig kidney but the reaction was negative when an alcoholic extract of beef heart was used as the antigen. The heterophile antibody present in this serum was absorbed by unheated and by heated sheep cells but not by human cells.

Lactic Acid in the Blood after Experimental Hemorrhage, and after Injection of Sodium Lactate in Dogs.—Cecilia Riegel (from the Department of Physiological Chemistry, School of Medicine, University of Pennsylvania). After severe hemorrhage there is a decrease in pH and in the alkaline reserve of the blood. These changes have been attributed by some to an increased production of lactic acid by the body, and by others to diffusion of alkali from blood to tissues. The experiments here reported support the first possibility.

Increased formation of lactic acid may occur when the oxygen supply to the tissues is inadequate. The transport of oxygen may be diminished after hemorrhage on account of constriction of peripheral blood-vessels, and the decrease in hemoglobin due to removal of a portion of the blood. We might expect, therefore, an increase in production of lactic acid after hemorrhage, resulting in an increased concentration of lactic acid in the blood. In order to study this possibility experiments were made in which normal dogs were bled 30 to 40 per cent of the blood volume. After hemorrhage samples of blood for analysis were taken at various intervals. In every case there was an increase in the concentration of lactic acid in the blood, the amount depending upon the extent of hemorrhage. When the hemorrhage was not extreme the highest lactic acid concentration was found at the end of the bleeding, followed by a gradual return to normal. When the hemor-

rhage was severe the lactic acid continued to increase for one to one and a half hours, and then began to return to normal. The decrease was always gradual. It depends upon restoration of an adequate oxygen supply, which prevents further formation of lactic acid, and upon the rate at which the chemical reactions involved in the removal of lactic acid proceed.

The disappearance of lactic acid from the blood after hemorrhage and after exercise suggested a study of its rate of removal when introduced into the body from an outside source. Amounts of lactic acid, as sodium lactate, varying from 0.85 gm. to 2.1 gm. were injected intravenously into dogs. The rate of disappearance from the blood, and the changes in inorganic phosphates were studied. Within five to ten minutes after the injection as much as two-thirds of the lactic acid had disappeared from the blood. The concentration was 60 to 80 mg. per 100 cc. as contrasted with a possible 100 to 300 mg. had all the injected lactic acid remained in the blood and been evenly distributed. Thirty minutes after the injection the rate of removal of lactic acid became much slower. Normal values were obtained only after one to two hours. The first rapid decrease is undoubtedly due for the most part to a diffusion of lactic acid from the blood into other body fluids. The inorganic phosphates of the blood decreased after the injection, the decrease being greater the larger the amount of sodium lactate injected. The coincident disappearance of phosphates and lactic acid suggests the formation of the hexose phosphate, lactacidogen. Urine analyses indicate only negligible quantities of the injected lactic acid are excreted.

The experiments on the whole indicate that lactic acid injected into the blood disappears rapidly, being synthetised to lactacidogen and glycogen just as is the lactic acid produced as the result of body metabolism.

Studies in Serum Electrolytes. II. The Electrolyte Composition and the pH of Serum of a Poikilothermous Animal at Different Temperatures.—J. H. AUSTIN, F. W. SUNDERMAN and J. G. CAMACK (from the John Herr Musser Department of Research Medicine, University of Pennsylvania). It has been established in mammals that at constant body temperature there is a tendency for the reaction of the blood to be maintained constant. This implies constant hydrogen-ion concentration, constant hydroxyl-ion concentration and constant amount of base bound per gram of any give protein. When the temperature of an aqueous solution such as blood is changed it is impossible for both hydrogen-ion and hydroxyl-ion concentrations to remain constant. It seemed important to determine under conditions of changing body temperature what would be the adjustment of the hydrogen-ion and hydroxyl-ion concentrations of the blood, whether one would be kept constant and if so which one, or whether there exists some other more fundamental biological relation which determines the resulting reaction of the blood.

In this study it was thought desirable to investigate an animal in which marked changes of body temperature can be induced physiologically. Accordingly, an animal was sought among the reptilia. With the assistance of Dr. Herbert Fox and of Mr. C. Emerson Brown

Director of the Gardens of the Philadelphia Zoölogical Society, the alligator was selected as suitable for the purpose and five of these animals and the facilities of Dr. Fox's laboratory were placed at the disposal of the John Herr Musser Department of Research Medicine. These animals were kept for periods of three or more days in water at from 7° to 10° C. At the end of these periods the animals had cloacal temperatures of from 8.5° to 9.8° C. The same animals were kept for other periods of three or more days in water at from 35° to 39° C. At the end of these periods they had cloacal temperatures from 34.6° to 36.0° C.

The serum of these animals showed at the higher temperature, as compared with the lower, marked increase in concentration of glucose and lactic acid, slight increase of protein, phosphate and chloride, and a higher CO_2 tension; no change or perhaps a slight diminution in total base, but marked diminution in bicarbonate.

The answer to the question under investigation, it is believed, was found in the fact that the reaction of the serum at both temperatures was such as to maintain constant the base bound by protein. This involves considerable change in hydrogen-ion concentration (pH_{9_0} = 7.72; pH_{35_0} = 7.27); a less marked change in hydroxyl-ion concentration (pOH_{9_0} = 6.73; pOH_{35_0} = 6.43). That the change in reaction with temperature should be that necessary to keept constant the base bound by protein is probably necessary in order to keep undisturbed the osmotic relation between tissue cells and serum.

On the Postnatal Growth in the Area of the Optic Nerve in Albino and in Gray Norway Rats.—H. H. DONALDSON (from the Wistar Institute of the University of Pennsylvania).

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